IN THE DISTRICT/~~SUPERIOR~~ COURT FOR THE STATE OF ALASKA
AT ANCHORAGE

Danielle-Susanne K. Wagner
Plaintiff(s),
vs.
Blue Cross Blue Shield of Illinois, A Division of Health Care Service Corporation, A Mutual Legal Reserve Company,
Defendant(s).

CASE NO. 3AN-14-9431 CI

SUMMONS AND
NOTICE TO BOTH PARTIES
OF JUDICIAL ASSIGNMENT

To Defendant: Blue Cross Blue Shield of Illinois, ~~Corporation~~, A Division of Health Care Service Corporation, A Mutual Legal Reserve Company

You are hereby summoned and required to file with the court a written answer to the complaint which accompanies this summons. Your answer must be filed with the court at 825 W. 4th Ave., Anchorage, Alaska 99501 within 20 days* after the day you receive this summons. In addition, a copy of your answer must be sent to the plaintiff's attorney or plaintiff (if unrepresented) Steve Jones, whose address is: P.O. Box 241546 Anchorage, AK 99524-1456.

If you fail to file your answer within the required time, a default judgment may be entered against you for the relief demanded in the complaint.

If you are not represented by an attorney, you must inform the court and all other parties in this case, in writing, of your current mailing address and any future changes to your mailing address and telephone number. You may use court form *Notice of Change of Address / Telephone Number* (TF-955), available at the clerk's office or on the court system's website at www.courts.alaska.gov/forms.htm, to inform the court. - OR - If you have an attorney, the attorney must comply with Alaska R. Civ. P. 5(i).

NOTICE OF JUDICIAL ASSIGNMENT

TO: Plaintiff and Defendant

You are hereby given notice that:

☐ This case has been assigned to Superior Court Judge _____ and to a magistrate judge.

☑ This case has been assigned to District Court Judge Olmstead.

CLERK OF COURT

11/6/2014
Date

SEAL OF THE TRIAL COURTS OF THE STATE OF ALASKA THIRD JUDICIAL DISTRICT

By: _____
Deputy Clerk

I certify that on 11/6/14 a copy of this Summons was ☐ mailed ☑ given to
☐ plaintiff ☑ plaintiff's counsel along with a copy of the
☐ Domestic Relations Procedural Order ☐ Civil Pre-Trial Order
to serve on the defendant with the summons.
Deputy Clerk _____

* The State or a state officer or agency named as a defendant has 40 days to file its answer. If you have been served with this summons outside the United States, you also have 40 days to file your answer.

STEVEN JONES
JONES LAW GROUP, LLC.
P.O. BOX 241546
ANCHORAGE, AK 99524-1456
565-5095

IN THE DISTRICT COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

DANIELLE-SUSANNE K. WAGNER,

Plaintiff,

vs.

BLUE CROSS BLUE SHIELD OF ILLINOIS, A DIVISION OF HEALTH CARE SERVICE CORPORATION, A MUTUAL LEGAL RESERVE COMPANY,

Defendant.

Case No.: 3AN-14-9431 CI

COMPLAINT

I. COMMON ALLEGATIONS

1. Danielle-Susanne K. Wagner ("Wagner") is a resident of Anchorage, Alaska.

2. Upon information and belief, Blue Cross Blue Shield of Illinois, a division of Health Care Service Corporation, a mutual legal reserve company ("Blue Cross") is a corporation located in Chicago, Illinois.

3. Blue Cross sells Medical Insurance throughout the country and is the medical insurance provider for McDonald's franchises.

4. For twenty years Wagner was insured by Blue Cross as a dependent under her father, John P. Wagner's insurance coverage with Blue Cross. Exhibit 1.

5. On or about April 23, 2012, Wagner received botox injections treatment for hyperhydroisis from Alaska Neurological Center LLC. Exhibit 2.

6. Blue Cross denied coverage for the botox treatments. Exhibit 3.

7. Wagner paid $2650.00 for the outstanding balance for the botox treatments. Exhibit 2.

8. The botox injections were ineffective. Wagner was referred to the Mayo Clinic for an endoscopic transthoracic limited sympathotomy for palmar/plantar hyperhidrosis. There was medical necessity for the treatment. Exhibit 3 and 4.

9. The outstanding balance for the treatments is $21,221.35. Exhibit 5.

10. Blue Cross denied payment for the Mayo Clinic surgical procedures on June 14, 2013. Exhibit 6.

11. Both the botox injections and the Mayo Clinic surgical procedures were medically necessary. Exhibits 10 and 11.

II. BREACH OF CONTRACT

12. Plaintiff realleges the above stated allegations.

13. Wagner entered into a contract with Blue Cross.

14. Blue Cross has breached its obligations under the contract by failing to pay for medical treatments as provided by

the medical coverage provided by Blue Cross's McDonald's Licensees & RMHC Health and Welfare Plan.

III. BREACH OF THE COVENANT OF GOOD FAITH AND FAIR DEALING

15. Plaintiff realleges the above stated allegations.

16. Every contract carries an obligation of good faith and fair dealing and Blue Cross's denial of Wagner's claim citing excuses that run contrary to the facts are a breach of the covenant of good faith and fair dealing.

III. BAD FAITH DENIAL OF INSURANCE COVERAGES

17. Plaintiff realleges the above stated allegations. Blue Cross has denied Wagner's insurance coverage in bad faith.

18. Blue Cross has breached its covenant to deal fairly and in good faith with Wagner and wrongfully denied payment of Wagner's medical providers.

19. Blue Cross's bad faith denial has resulted in Wagner's credit being effect as the outstanding medical bill are being referred to collection.

VII. CLAIMS MADE PURSUANT TO A.S. 45.50.531- UNFAIR AND DECEPTIVE TRADE PRACTICES

20. Plaintiff realleges the above stated allegations.

21. Blue Cross's actions and denial of benefits to Wagner through the course of all dealing described herein that were unfair and deceptive.

22. Blue Cross's omissions or misleading statements were made in the course of commerce and were unfair and deceptive.

23. Wagner relied upon these unfair and deceptive statements.

24. The deceptive and unfair practices of Blue Cross were performed willfully and entitle the Taylors to treble damages.

VII. CLAIMS MADE PURSUANT TO A.S. 21.36.125- UNFAIR CLAIM SETTLEMENT PRACTICES

25. Plaintiff realleges the above stated allegations.

26. Blue Cross's actions and denial of benefits to Wagner through the course of all dealing described herein that were an unfair denial of health insurance benefits.

27. Blue Cross's omissions or misleading statements were made in the course of commerce and were unfair and in bad faith.

28. Wagner relied upon Defendant to fairly settle her claims for benefits under her policy.

29. The unfair and bad faith practices of Blue Cross were performed willfully and entitle Wagner to treble damages.

VIII PRAYER FOR RELIEF

Plaintiffs request judgment against the Defendant as follows:

1. For an order requiring Blue Cross to pay for Plaintiff's Botox injection treatments and Mayo Clinic surgery.
2. For an award of treble damages for bad faith insurance claim denial.
3. For an award of treble damages pursuant to the Unfair Trade Practices Act.

4. For an award of treble damages pursuant to the Unfair Claims Settlement Practices Section 21.36.125.

5. For an award of punitive damages.

6. For an award of pre-judgment and post-judgment interest at the contract rate where applicable and for attorney's fees as provided by contract and/or law.

7. For attorney fees and costs.

8. For any other relief this court deems just and proper.

Attorney for Plaintiff

9-22-14
Date

Steven Jones
93-11102
907-565-5095

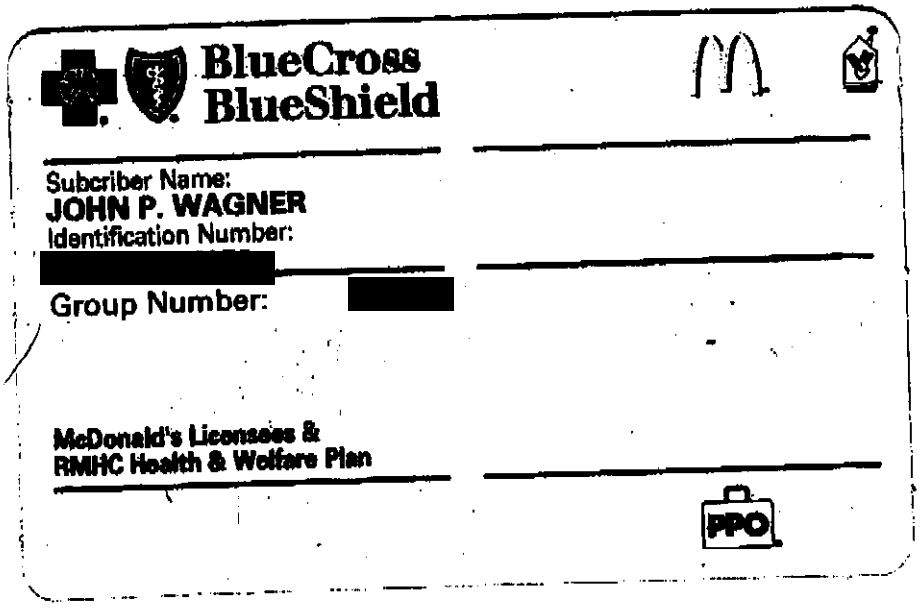


EXHIBIT 1

PAGE 1 OF 2

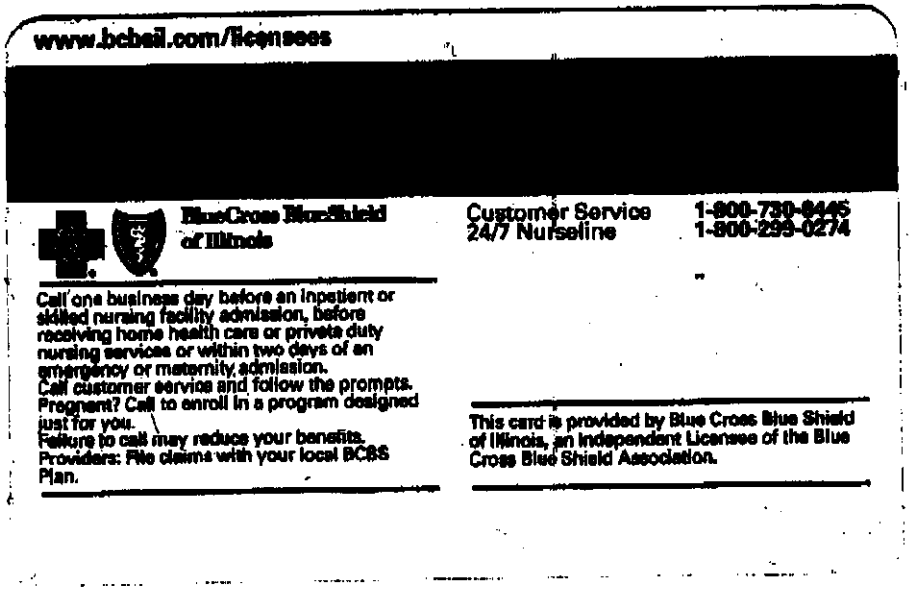

www.bcbsil.com/licensees
[redacted]
BlueCross BlueShield of Illinois
Customer Service 1-800-730-8445
24/7 Nurseline 1-800-299-0274
Call one business day before an inpatient or skilled nursing facility admission, before receiving home health care or private duty nursing services or within two days of an emergency or maternity admission.
Call customer service and follow the prompts.
Pregnant? Call to enroll in a program designed just for you.
Failure to call may reduce your benefits.
Providers: File claims with your local BCBS Plan.
This card is provided by Blue Cross Blue Shield of Illinois, an Independent Licensee of the Blue Cross Blue Shield Association.

EXHIBIT 1

ALASKA NEUROLOGY CENTER LLC

Patient Ledger

July 14, 2014

SUSAN WAGNER
[redacted]

Account Number: [redacted]
Work Phone:
Home Phone: [redacted]

Date	Patient	Bill No.	Description	Amount
12/19/2011	DANIELLE	25226	99243 - OFFICE CONSLTJ 40 MIN	$485.00
01/20/2012	DANIELLE	25226	P1 - PRIMARY INSURANCE PAYMENT	($385.00)
12/19/2011	DANIELLE	25226	P6 - PATIENT PAYMENT - CREDIT CARD	($113.00)
01/20/2012	DANIELLE	25226	W4 - BCBS CONTRACTUAL WRITE-OFF	($70.00)
	BILLED: BCBS 12/23/2011		Total for Bill No. 25226	($103.00)
03/12/2012	DANIELLE	27185	99214 - OFFICE OUTPT EST LVL IV	$385.00
04/06/2012	DANIELLE	27185	P1 - PRIMARY INSURANCE PAYMENT	($231.00)
04/06/2012	DANIELLE	27185	W4 - BCBS CONTRACTUAL WRITE-OFF	($154.00)
	BILLED: BCBS 03/15/2012		Total for Bill No. 27185	$10.00
04/23/2012	DANIELLE	28164	J0585 - BOTULINUM TOXIN TYPE A, PER UNIT	$2,800.00
04/23/2012	DANIELLE	28164	64650 - CHEMODNRVTJ ECCRINE GLNDS BTH AX	$1,250.00
04/23/2012	DANIELLE	28164	W7 - PROVIDER AUTHORIZED WRITE-OFF	($1,400.00)
04/23/2012	DANIELLE	28164	P6 - PATIENT PAYMENT - CREDIT CARD	($2,650.00) ✓ PAID
	BILLED: BCBS 10/03/2012		Total for Bill No. 28164	$0.00
11/12/2012	DANIELLE	32991	99213 - OFFICE OUTPT EST LVL III	$285.00
12/06/2012	DANIELLE	32991	P1 - PRIMARY INSURANCE PAYMENT	($184.00)
12/06/2012	DANIELLE	32991	W4 - BCBS CONTRACTUAL WRITE-OFF	($91.00)
	BILLED: BCBS 11/21/2012		Total for Bill No. 32991	$10.00
			Estimated Insurance Responsibility	$0.00
			Estimated Patient Responsibility	($83.00)

Current	> 30 Days	> 60 Days	> 90 Days	> 120 Days	Balance
($83.00)					($83.00)

Report Totals

Current	> 30 Days	> 60 Days	> 90 Days	> 120 Days	Report Balance
($83.00)					($83.00)

ProdigyMD

EXHIBIT 2

PAGE 1 OF 1

BlueCross BlueShield
of Illinois

March 01, 2012

John Wagner
[redacted]

Subscriber: John Wagner
Member: Dani Sue Wagner
Group/ID#: [redacted]
Beginning Date of Claims:
Ending Date of Claims:
Service: proposed Botox
Case Number: 55959001

Dear John Wagner:

This letter is in response to your request for an appeal of the denial of benefits for proposed Botox.

A physician who specializes in Dermatology and who had no involvement in the original denial reviewed your request and the available clinical information. Based on this review, the following determination has been made:

Summary of Records: This is a 17 year old patient for whom Botox is under review.

Decision: Do not approve benefit reimbursement for proposed Botox, billing code J0585.

Reason: The patient does not meet the BCBSIL Medical Policy criteria for coverage of this service.

The patient does not have acrocyanosis. The patient does not have skin maceration with bacterial or fungal infections. The patient does not have secondary infections due to her axillary hyperhidrosis. The patient is not noted to have persistent eczematous dermatitis. Therefore per the BCBSIL guidelines, the patient does not meet criteria set up to establish medical necessity of Botox for axillary hyperhidrosis.

There are no extenuating circumstances such that the service is medically necessary for this member. The patient does have axillary hyperhidrosis that has failed first line topical therapy. However she does not have any secondary health problem.

Upon request, the physician, facility, health care provider, member or member representative may have access to a copy of the clinical rationale, medical criteria or benefit provision used to make the determination, as well as copies of documents relevant to the appeal.

EXHIBIT 3.

Please refer to your member booklet, Health Care Benefit Program description or member's Certificate to determine if additional levels of appeal are available to you.

We have denied your benefits request for the provision of, or payment for, a health care service or course of treatment. You have the right to have our decision reviewed by an independent review organization not associated with us, if our decision involved the following:

- making a judgment as to the medical necessity and the appropriateness of the; requested service;
- health care setting;
- the level of care; or
- the effectiveness of the health care service or treatment you requested

You can submit a written request for an external review directly to us. Upon receipt of your request an independent review organization registered with the Illinois Department of Insurance will be assigned to review our decision. Please see the attached Appeal request Information and Procedures instructions for requesting an external review.

Blue Cross and Blue Shield of Illinois (BCBSIL) operations are regulated by the Illinois Department of Insurance. If you wish to take up this matter with Illinois Department of Insurance, it maintains a Consumer Division in Chicago at 100 W. Randolph Street, Suite 15-100, Chicago, Illinois 60601-1115 and in Springfield at 320 W. Washington Street, Springfield, Illinois 62767-0001. The Illinois Department of Insurance, Consumer Division, can be contacted by telephone toll free at 1-877-527-9431.

In addition, you have the right to bring a civil action under section 502(a) of ERISA following an adverse determination of review, provided you are in a group insurance plan that is not a government or church group.

If you have additional questions, please contact me at 312/653-8507.

Sincerely,

Jennifer Arevalo
Quality Review Specialist
Appeals Department
Consumer Services Management

Cc: Cathy McClain-Gordon, Senior Director, Consumer Services Management
Alaska Neurology Center

Attachment:
IDOI Request for External Review Form

EXHIBIT 3

MAYO CLINIC

200 First Street SW
Rochester, Minnesota 55905
507-284-2511
mayoclinic.org

John L. Atkinson, M.D.
Department of Neurologic Surgery

✓ January 20, 2014

RE: Ms. Danielle-Susanne K. Wagner
MC#: [redacted]
DOB: [redacted]

To Whom It May Concern:

Ms. Danielle-Susanne Wagner (Group [redacted]; ID [redacted]) has shared with us your letter dated June 14, 2013, stating her sympathomy was denied coverage for 'lack of medical necessity'. I wish to emphasize that this was not a cosmetic procedure, but a surgical procedure to treat a medical affliction, which incapacitates patients' lives for a significant myriad of reasons. We are writing on Ms. Wagner's behalf in the hope you would overturn your decision.

Enclosed please find consultation notes from Dr. Lawrence Gibson in Dermatology, Dr. Michel Toledano and Dr. Michelle Mauermann from Medical Neurology and from my visit with her. We am also enclosing her thermoregulatory sweat test results showing acral hyperhidrosis and normal distribution of sweating which predicts good surgical outcome. Likely these were previously provided to you, but I wish to point out some salient features:

1) She has had the condition for many years and had been evaluated and treated by a dermatologist in Alaska. This physician had tried her on oral agents, which were not effective, and also topical Drysol which produced skin irritation without treating the hyperhidrosis.

2) Botox injections were tried once in each axilla. This brought some improvement but not complete treatment, and also only lasted for 2-3 months, which is common. For use in palmar hyperhidrosis, we submit that Botox treatments are expensive and since they are temporary, would need to be repeated ongoing throughout her life. The surgery is a permanent solution. We would also add that the risk of any hand weakness could interfere with her ability to work as a paramedic. We also know they are not a total solution (e.g. injections are not made between the fingers which means the patient's hands may not be completely dry even under the best of circumstances); and also, antibodies can develop. We refer you to the section about botulinum toxin on page 661 of the enclosed summary article by Doctor Eisenach on hyperhidrosis.

EXHIBIT 4

(7-354-496) Ms. Danielle-Susanne K. Wagner

3) Your letter elaborates that no documentation of skin conditions was provided. As stated above, the Drysol did provoke a rash and her hands were at risk for ongoing fungal infections from the moisture alone. As a paramedic, she also needs to wear gloves which would increase her risk of skin maceration and infection. On that basis, we would think an insurance company would feel it prudent to consider sympathotomy prior to the patient having any further medical condition of the skin.

4) Last, but not least, functional disability is most often listed as a medically necessary reason for treatment of hyperhidrosis. Palmar hyperhidrosis is incapacitating when severe, as Ms. Wagner's was. We believed her case was best handled by surgery based on clinical evidence in the history and physical by her home dermatologist, Dermatology, Neurology and Neurosurgery at Mayo Clinic. In this day and age of electronic touch devices such as IPads, it is important to note that having wet hands interferes greatly with the use of such devices.

We are enclosing two peer-reviewed journal articles as reference points. We will also send a copy of an editorial from the New York Times that summarizes care here at the Mayo Clinic compared with other nationally known medical institutions and their impression of our care. Of note, there is no profit motivation on my part, as we are salaried here at the Mayo Clinic from the clinician standpoint.

We have written on behalf of other BCBS Illinois patients in the past and you and a Medical Director, Dr. Dawn Warren, have been amenable to approving those patients, so we hope you will provide this same service to Ms. Wagner. If you have any questions or concerns, please feel free to contact me at anytime. I would be happy to speak with the Medical Director assigned to Ms. Wagner's case on her behalf. I can be contacted at (507) 284-2376.

Signed: _____
John L. D. Atkinson, M.D.

jla/laf
Enclosures

cc: Ms. Danielle-Susanne Wagner
[redacted]

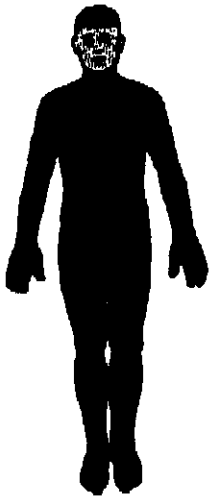
Thermoregulatory Sweat Test

Patient: **WAGNER, DANIELLE**

ID: [redacted]

Desk: **GOBS** Age: **18** Sex: **F** Date/Time: **03/11/2013 08:00**

Indication: **HYPERHIDROSIS**



Sweating in purple shaded area

RESULTS

Oral temp before: **36.6** °C after: **37.3** °C

%anhid: **0.9**

Distribution: **HYPERHIDROSIS**

IMPRESSION

There was preheat sweating over palms, soles and axillaes, consistent with acral hyperhidrosis.

Physician: **P. SANDRONI M.D.**

Pager: **4-7174**

11-Mar-2013 - Consult, John L D Atkinson, Neurosurgery

REFERRAL
Michelle L. Mauermann, M.D. (4-6689).

CHIEF COMPLAINT/PURPOSE OF VISIT
Sweaty palms.

HISTORY OF PRESENT ILLNESS
This is an 18-year-old woman referred by Dr. Mauermann with severe type I essential palmar plantar hyperhidrosis who has failed all conservative management strategies and now wishes a surgical consultation for her condition.

IMPRESSION/REPORT/PLAN
I have reviewed the results of her thermoregulatory sweat test, which confirm her condition, and also the history well-defined by Dr. Mauermann but also Dr. Gibson in Dermatology as well. Given the severity of her condition and refractory nature to all her medical pursuits at treatment strategies, she would be a good surgical candidate.

The surgical consent form was signed and witnessed and will be scanned into her records today.

The roles and responsibilities of my surgical team members were also discussed, and she has checked no, not interested to advance directives.

The thermoregulatory sweat test was reviewed, and the educational material was also reviewed and given to the patient and her mother and documented on the flowsheet. They wish to pursue tomorrow, and we will make arrangements accordingly.

INFORMED CONSENT
Using the thermoregulatory sweat test and our educational material, I discussed the risks, goals, and alternatives of bilateral transthoracic sympathotomy in detail with the patient and her mother. I discussed a 96% long-term dry hands result, which is our series over the last 20 years, and a very low complication rate. Specifically, 96% of patients will have dry hands for life, and 4% of patients fail the procedure within the first three years. Seventy percent of patients have drier armpits, and 40% of patients have drier feet, though neither of these areas are as dry as the hands.

The risks are 1% chance or less of having bleeding occur during the procedure that may be life-threatening and require a thoracotomy to repair. There would be a 1% chance of needing a chest tube for hemopneumothorax. The other risks are both cosmetic, and I discussed a Horner's syndrome and severe compensatory hyperhidrosis in detail. All questions were answered, there were no barriers to our discussion, and the patient and her mother fully understand.

Original: jla/hdo
Electronically Signed: 22-Mar-2013 05:57 by J.L. Atkinson, MD

11-Mar-2013 - Supervisory, Michelle Lynn Mauermann, Neurology

REFERRAL
Lawrence E. Gibson, MD (4-7877), Dermatology.

CHIEF COMPLAINT/PURPOSE OF VISIT
Assisted by: Michel Toledano, M.D. (127-10149).

HISTORY OF PRESENT ILLNESS

I have reviewed Dr. Michel Toledano's (127-10149) history, examination, and plan of care as documented on the electronic neurologic examination and history. I have personally interviewed and examined the patient. I agree with Dr. Michel Toledano's documentation, other than where indicated in my note.

Ms. Wagner is an 18-year-old whom I am seeing today in Peripheral Nerve Clinic at the request of Dr. Gibson for evaluation of hyperhidrosis. She has a positive family history of hyperhidrosis in her biological grandmother and her 8-year-old sister. Her two twin brothers are unaffected. She developed her symptoms primarily when she went through puberty and started menses and developed acral hyperhidrosis. Her symptoms are most prominent in the palms and soles and in her armpits. She has tried Drysol which gave her a rash as well as Botox with modest results. They helped with the daily day-to-day but not with any particular triggering stressful situations. She has some orthostatic light-headedness with palpitations. Otherwise no significant problems.

The TST today showed acral hyperhidrosis of the palms and soles and mildly in the armpits. There are no areas of hypohidrosis or anhidrosis. She also has a goiter but right now has normal TSH and a free T4 so unlikely to be associated.

PHYSICAL EXAMINATION

Neuro: Neurological exam was normal apart from some mild postural tachycardia and acral hyperhidrosis.

IMPRESSION/REPORT/PLAN

#1 Essential hyperhidrosis
#2 Possible postural tachycardia/orthostatic intolerance

Agree with Dr. Toledano to get an autonomic reflex screen given the postural tachycardia to make sure there is no other autonomic dysfunction here. Otherwise she appears to be a good candidate for surgical consultation having failed Drysol and Botox and having a sweat test that is very characteristic for essential hyperhidrosis. We will go ahead and make the referral to Dr. John Atkinson for evaluation.

DIAGNOSES

#1 Essential hyperhidrosis
#2 Possible postural tachycardia/orthostatic intolerance

Original: mlm/dma revised by mlm
Electronically Signed: 12-Mar-2013 13:23 by M.L. Mauermann, MD

11-Mar-2013 - Consult, Michel Toledano, Neurology

CHIEF COMPLAINT/PURPOSE OF VISIT

Patient was seen in conjunction with Dr. Mauermann (4-6689).

HISTORY OF PRESENT ILLNESS

Ms. Wagner is an 18-year-old woman from Anchorage, Alaska, who presents to the Peripheral Nerve Clinic today at the request of Dr. Gibson for evaluation of hyperhidrosis.

Ms. Wagner is accompanied by her mother. They tell me that Danielle has had symptoms since she was a small girl. As a little girl, she was always hot and did not want to wear sweaters or heavy jackets. When she reached puberty, she began to notice that she was sweating more than her friends. This became much worse after the onset of menses. She primarily has symptoms in her hands, feet, and axilla. She will sweat profusely at baseline, but this will get worse with heat, physical activity, or anxiety.

Ms. Wagner is adopted but lives with her biological sisters and twin brothers. They are all from the same mother but different fathers. The biological mother's mother also suffers from hyperhidrosis, and it

appears that Danielle's little sister, who is currently 8, is also developing symptoms.

She has tried Drysol, which gave her a rash, as well as Botox injections with only modest results.

She has a history of irregular menses with heavy bleeding, but this has improved with oral contraceptives. She also has a history of orthostatic light-headedness and palpitations.

She underwent a thermoregulatory test today which showed acrohyperhidrosis of the palms, soles, and mildly in the armpits. There were no areas of hypohidrosis are anhidrosis. She also has a goiter, status post biopsy. This is likely benign. TSH and free-T4 are normal. She is currently undergoing evaluation by Endocrinology here.

VITAL SIGNS

Blood Pressure: Position/Cuff: . Pulse Rate: 62/minute, sitting. (11-Mar-2013 10:34)
Blood Pressure: Position/Cuff: . Pulse Rate: 93/minute, standing. (11-Mar-2013 10:35)

PHYSICAL EXAMINATION

General: Vitals: Orthostatic blood pressure measurements were obtained. There were no drops in the blood pressure, but heart rate went from 62 when sitting to 93 when standing. The patient was asymptomatic.
Gait: Examined and normal.
Neuro: Please see my CDM report for details.
There were no cognitive abnormalities noted.
Speech and language were normal.
Cranial nerve exams were normal.
She did have hippus.
On motor exam, there was no detectible weakness.
Reflexes were equal and symmetric.
Toes were flexor.
Coordination was normal.

On sensory exam, she did have minor subjective pinprick loss in the feet bilaterally.

IMPRESSION/REPORT/PLAN

#1 Hyperhidrosis
#2 Query postural tachycardia/orthostatic intolerance

Ms. Wagner has a normal neurologic exam. Given the history of orthostatic intolerance and change in heart rate, I think an autonomic reflex screen would be reasonable to make sure there is no other autonomic dysfunction present, although I think this likely will be normal.

She is a good candidate for surgical consultation as she has failed Drysol and Botox injection. Her TST is very characteristic of essential hyperhidrosis. We will make a referral to Dr. John Atkinson for evaluation.

DIAGNOSES

#1 Hyperhidrosis
#2 Query postural tachycardia/orthostatic intolerance

Original: mt/kls revised by hml
Electronically Signed: 15-Mar-2013 17:30 by M.. Toledano, MD

8-Mar-2013 - Consult, Lawrence Edward Gibson, Dermatology

REFERRAL

Margretta A. O'Reilly, M.D.
3841 Piper Street, Ste. T04-020
Anchorage, AK 99508

HISTORY OF PRESENT ILLNESS

The patient is seen for the first time in the Department of Dermatology. Danielle is accompanied by her mother today. Her major reason for coming to the Mayo Clinic is for hyperhidrosis, but she also has had issues with a goiter involving her thyroid gland for the past two years, and she wonders whether or not the two might be connected with one another. The patient has seen a dermatologist at home and has undergone therapy for hyperhidrosis, which at this time is primarily the problem in the axillary area but also has been a problem on the palms as well. She has not had significant problems of the scalp or on the truncal area or on the feet to the same degree she has in the axillary area. Treatments have consisted of oral anxiolytic agents, which were not effective. She has also had aluminum hexachloride topical treatments such as Drysol which caused irritation but were not very effective. More recently in 2012, she had injections of Botox in each axilla, which did bring about some improvement but they were not completely effective and this effectiveness lasted for only about two to three months before it dissipated. Patient has not used Drionic unit up to this point. She is referred also for the problem of her thyroid gland, which has been enlarged now for about three years. Biopsy was done in the fall of 2010, which evidently was benign, but no additional treatment has been recommended for this problem. Patient says she also develops from time to time protuberances on the anterior legs, which become worse with exercise. These are not tender but are somewhat bothersome to the patient. Otherwise, she appears to be in a good state of general health.

SYSTEMS REVIEW

Other than noted above, the patient appears to be in good general state of health and has had no other significant health issues.

SOCIAL HISTORY

The patient lives with her family in Alaska and attends the college there where she commutes back and forth. She is interested in studying to become a paramedical and appears to be adjusted well socially.

FAMILY HISTORY

The patient is accompanied by her adoptive mother, but her biologic grandmother is known to have hyperhidrosis, especially involving the scalp area. There are some issues in her biologic family with anxiety, but otherwise her family history is not extensively known.

PHYSICAL EXAMINATION

Skin: Examination today demonstrates that the patient appears to be fairly relaxed in a good state of general health. She has no overt skin abnormalities on the palms or the upper extremities nor in the axillary area. Her axilla and palms are moist with perspiration but not excessively so considering the situation she is in at this time. I examined her legs, and there appears to be either a slight protuberance of fatty tissue similar to a piezogenic papule or perhaps a prominence of a vein in this area, but I do not detect any changes that would suggest thyroid-related abnormality of the skin of the leg. Otherwise, examination demonstrates that she has obvious enlargement of her thyroid gland. Left lobe appears to be enlarged greater than the right, but it is quite obvious when she swallows that her gland is enlarged. Otherwise, examination is unremarkable.

IMPRESSION/REPORT/PLAN

#1 Goiter

I believe the patient most likely has a benign goiter but given her other complaints of hyperhidrosis and the complaints regarding the skin of her legs, I believe it would be most appropriate for our specialists here in the Thyroid Clinic to evaluate her and to make sure she does not require another biopsy and to also see whether or not she requires any therapy. I would also appreciate their opinion as to whether or not her thyroid abnormalities would have anything to do with her hyperhidrosis.

#2 Hyperhidrosis

I believe the patient should undergo sweat test in addition to the consultation and examinations above. Based on the results of the sweat test, consultation with a small fiber neurologist may also be appropriate. Therapeutic options, assuming there is no other primary cause found for this problem, would include excision of the affected areas in the axillary area or transthoracic sympathectomy. I discussed with the patient and her mother briefly both of these procedures and further discussion can take place with the appropriate specialist if and when the decision is made to proceed in this direction.

Questions answered.

Original: leg/wsr revised by val
Electronically Signed: 11-Mar-2013 10:02 by L.E. Gibson, MD

CONCISE REVIEW FOR CLINICIANS

Hyperhidrosis: Evolving Therapies for a Well-Established Phenomenon

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The socially embarrassing disorder of excessive sweating, or hyperhidrosis, and its treatment options are gaining widespread attention. In order of frequency, palmar-plantar, palmar-axillary, isolated axillary, and craniofacial hyperhidrosis are distinct disorders of sudomotor regulation. A common link among these disorders is an excessive, nonthermoregulatory sweat response often to emotional stimuli in body regions influenced by the anterior cingulate cortex as opposed to the thermoregulatory sweat response regulated by the preoptic-anterior hypothalamus. Diagnosis of these mechanistically ambiguous disorders is primarily from patient history and physical examination, whereas results of laboratory studies performed with indicator powder reveal the distribution and severity of resting hyperhidrosis and document the integrity of thermoregulatory sweating. Treatment options lie on a continuum based on the severity of hyperhidrosis and the risks and benefits of therapy. In general, therapy begins with antiperspirants or anticholinergics. Iontophoresis is available for palmar-plantar and axillary hyperhidrosis. Botulinum toxin type A or local excision/curettage is effective for isolated axillary hyperhidrosis not responsive to topical application of aluminum chloride. Endoscopic thoracic sympathectomy may be used for severe cases of palmar-plantar and palmar-axillary hyperhidrosis. No sole therapy of choice has emerged for craniofacial sweating. The long-term sequelae of hyperhidrosis and its treatment also are discussed.

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BT-A = botulinum toxin type A; CH = compensatory hyperhidrosis; ETS = endoscopic thoracic sympathectomy; TST = thermoregulatory sweat test

Excessive sweating, or hyperhidrosis, is a socially embarrassing disorder that may seem trivial to the general public because of its falsely perceived rarity; however, hyperhidrosis is being recognized increasingly, and its treatment options are gaining widespread attention.[1-3] Both ancient and modern medicine have been perplexed by this entity. Of sweating, Hippocrates used the term *hidroa*, which was translated from Greek into Latin and English as *sudamina*. Both terms gave rise to the present use of *hidrosis* and *sudomotor function*.[4] Nearly 100 years ago, Meachen[5] described hyperhidrosis and 3 therapeutic goals that have withstood time: "...1) To seek out the underlying cause for the increased sweating and endeavor to remove it; 2) to check or modify the amount of secretion itself; and 3) to relieve any secondary dermatitis or other complications that may arise."

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A question-and-answer section appears at the end of this article.

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DEFINITIONS

The condition that results when the sudomotor system (which controls sweat output) functions excessively in isolation with no apparent cause is termed *primary* or *essential hyperhidrosis*. It is imperative to differentiate this condition from *secondary hyperhidrosis*, which can be associated categorically with infection, malignancy, neurologic and endocrine disorders, spinal cord injury, and miscellaneous causes (Table 1).[6] An important contemporary cause, terrorism-related chemical warfare agents (such as organophosphate compounds that inhibit acetylcholinesterase, similar to agricultural pesticides), must be included in this list.[7]

Primary hyperhidrosis is classified as focal or generalized on the basis of the stimulus and site of neuromodulation. The exaggerated sweating response to emotional or sensory stimuli probably originates in the anterior cingulate frontal cortex as opposed to thermoregulatory sweating, which is primarily regulated by the preoptic-anterior hypothalamus.[8] Focal hyperhidrosis most commonly affects the palms (Figure 1, top) and soles. Excess sweating in these areas is called palmar-plantar hyperhidrosis. Isolated axillary hyperhidrosis affects only the underarms and may coexist with palmar-plantar hyperhidrosis. Finally, and least common, there is isolated supranormal sweating of the face (craniofacial hyperhidrosis), which may be provoked by heat, emotion, or spicy foods (gustatory hyperhidrosis). This disorder is difficult for patients to hide, especially if the facial skin forms a darkened hue called chromhidrosis.

EPIDEMIOLOGY

A recent survey in the United States suggests that the prevalence of primary (essential) hyperhidrosis is 2.8%, with approximately one half (1.4%) of these individuals projected to have axillary hyperhidrosis and one sixth (0.5%) projected to have sweating that is intolerable or interferes with daily activities.[9] Epidemiological data spe-

TABLE 1. **Categories of Secondary Hyperhidrosis**

Category	Pathogenesis	Features
Chronic infection	Tuberculosis, brucellosis	Night sweats
Neuroendocrine malignancy	Pheochromocytoma	Paroxysmal sweating, sudomotor cholinergic activation from excess catecholamines; responds to anticholinergics
Endocrinologic	Thyrotoxicosis, diabetes mellitus	Paroxysmal sweating, increased metabolism and increased sensitivity of nerve fibers to epinephrine; thyrotoxicosis responds to β-blockade
Malignancy	Leukemia, lymphoma, renal cell carcinoma, Castleman disease	Night sweats, pruritus; may respond to plasmapheresis or histamine$_2$ receptor antagonists
Neurologic diseases	Acromegaly, carcinoid syndrome, diencephalic epilepsy, basilar artery occlusion–pontine ischemia	Paroxysmal sweating; pontine ischemia may damage descending inhibitory fibers
Biochemical agents	Acetylcholinesterase inhibitors, chemical warfare, pesticides	Responsive to removal of stimulus, anticholinergics
Spinal cord injury	Autonomic dysreflexia, orthostatic hypotension, posttraumatic syringomyelia	Can occur months to years after injury to spinal cord
Miscellaneous	Anxiety, hypoglycemia, menopause	

cific to palmar hyperhidrosis are sparse, but this condition affects an estimated 0.6% to 1.0% of the Western population.[10] The prevalence of severe palmar hyperhidrosis varies geographically and has been described as endemic in Southeast Asia, where it affects up to 3% of the population.[10,11] This high prevalence in Southeast Asia can be seen in the staggering group sizes (1167-9988 patients) in several outcome studies of thoracoscopic sympathectomy.[12-14] On review of these and other large-scale reports,[12-17] several conclusions can be drawn. Of patients with severe hyperhidrosis presenting for surgery, most have palmar-plantar hyperhidrosis, 15% to 20% have combined palmar-axillary hyperhidrosis, 5% to 10% have isolated axillary hyperhidrosis, and less than 5% have craniofacial hyperhidrosis. Hyperhidrosis is heritable in autosomal dominant fashion with variable penetrance; a recent study on allelic probability estimates that a child of a parent with palmar hyperhidrosis has a likelihood of phenotypic expression of 0.28, meaning the child has an approximate 25% chance of developing hyperhidrosis.[18] Most large studies report that 25% to 50% of patients with palmar hyperhidrosis have a family history of the disorder. No other risk factors are known to cause primary hyperhidrosis.

MECHANISMS

Understanding why patients have supranormal sweating of the hands and feet begins with understanding the complex interaction between thermoregulatory sweating and emotional sweating. Thermoregulatory sweating is the major mechanism of heat dissipation by whole-body eccrine glands, is controlled by the preoptic area of the hypothalamus, and is diurnal or nocturnal. Emotional sweating, always diurnal, is controlled by the anterior cingulate cortex, and its distribution is limited usually to the face, axillas, palms, and soles.[8] Both higher centers descend to synapse on the intermediolateral cell column neurons of the spinal cord. From there, myelinated preganglionic sympathetic nerves exit the cord via the ventral roots and enter the segmental paravertebral sympathetic ganglia or course up and down the sympathetic chain and enter paravertebral ganglia at other levels. Unmyelinated postganglionic sympathetic fibers exit the ganglion and rejoin the segmental spinal nerve or plexus, eventually innervating pilomotor (hair follicles), sudomotor (sweat glands), and vascular effectors of the skeletal muscle and skin of the trunk and limbs.

Sudomotor nerves release acetylcholine onto the muscarinic cholinergic receptors of the sweat glands (Figure 2). There are 2 million to 5 million sweat glands in the body, and they are anatomically and functionally differentiated into eccrine and apocrine. Developed in utero, eccrine sweat glands are ubiquitous in skin but are heavily concentrated in the forehead, scalp, axillas, palms, and soles.[19] Glabrous or hairless skin (palms, soles, lips) is rich in arteriovenous anastomoses (bypass conduits between arterioles and venules) that are richly innervated by sympathetic vasoconstrictor nerves.[20] Thus, in addition to emotional sweating, glabrous skin is a source of thermoregulation and heat release. In the dermis, eccrine gland secretory coils secrete an isotonic, slightly acidic solution (with sodium, potassium, and chloride ions) into the sweat ducts, which reabsorb sodium chloride and produce hypotonic sweat destined for the epidermis. The apocrine glands are small and inactive until puberty, when they become larger and produce a secretion thicker than sweat. Localized to the

axilla, areola of the nipple, and perineum in humans, apocrine gland secretion is of little physiological importance; in other mammals, it may function as a sexual attractant.

In nonhyperhidrotic individuals at normal body temperature in a comfortable environment, the low level of sweat production in the eccrine glands of the palms and soles is controlled by the neocortical emotional component. As the temperature increases, hypothalamic thermoregulatory control of nonglabrous skin is activated primarily with minor effects on palmar and plantar sweating. If mental stress is added to the setting of heat stress, palmar and plantar sweating increases further.[21] In palmar hyperhidrosis, a hyperfunctioning, emotional component of the central sudomotor nervous system occurs, evidenced by the observation that excess sweating does not occur during sleep and is aggravated by emotional stimuli. During mental stress, increased skin sympathetic nerve activity and pronounced vasoconstriction,[22] excessive sweating,[23] and an associated increase in evaporation[24] collectively cause cold, "clammy" hands. There is pronounced vasoconstriction of the hand with a markedly low cutaneous temperature at rest, which is exaggerated during cooling maneuvers.[25-27] Furthermore, sweating is excessive during exercise[25] and whole-body heating, suggesting a hyperfunctioning hypothalamic thermoregulatory component that compounds the emotional component of sweating.[28] Finally, regional anesthesia injections on the ulnar nerve of a patient with palmar hyperhidrosis produce warm, dry skin in dermatomal fashion.[23] Together, these findings suggest that primary hyperhidrosis (1) is most likely caused by hyperfunctioning central sudomotor output, (2) has a predominantly emotional component, (3) is associated with a more tonically active sympathetic innervation of vasomotor downstream effectors and a more labile innervation of sudomotor effectors, and (4) can be ameliorated by sympathetic denervation.

FIGURE 1. A young, healthy patient with primary palmar-plantar hyperhidrosis in resting conditions at room temperature. Top, A mixture of starch, alizarin red, and sodium carbonate is placed on the palms of a hyperhidrotic patient at rest whose core temperature is then elevated, changing the indicator color from light orange to purple. Bottom, Test is repeated in the same patient under the same conditions 2 months after successful endoscopic thoracic sympathotomy (see text).

DIAGNOSIS

Patient History and Examination

A substantial part of the diagnosis of hyperhidrosis can be achieved by obtaining a patient history. Patients describe excessive sweating that began in childhood or adolescence. Palmar hyperhidrosis interferes with nearly all tasks of manual dexterity. Avoidance of handshake can lead to professional embarrassment, and avoidance of touch can lead to social or interpersonal seclusion. These symptoms put patients at risk for higher levels of disability, fear, avoidance, and other physiological symptoms (blushing, trembling) that may encompass social anxiety disorder.[29] Palmar hyperhidrosis usually is accompanied by plantar hyperhidrosis, which is easier to conceal but when extreme may cause bromhidrosis (foul-smelling sweat), infection, and skin maceration. Isolated axillary hyperhidrosis is more indicative of abnormal apocrine and eccrine sweating under both thermoregulatory and emotional control. Patients with this disorder change clothing repeatedly and usually have already explored numerous over-the-counter antiperspirants. Gustatory hyperhidrosis can be a normal response to certain foods, whereas the rare primary craniofacial hyperhidrosis is provoked by emotional and environmental stimuli similar to palmar-plantar hyperhidrosis.

Clinical Laboratory Testing

Once secondary causes of hyperhidrosis have been ruled out, dermatologic and/or autonomic laboratories have several techniques to stratify the severity of sweating. The Minor starch-iodine test delineates the area of sweating using iodine solution, 3.5% in alcohol, applied to clean, dry shaved skin.[30] Dry starch powder is applied lightly; sweat causes the mixture to turn dark blue, highlighting the loca-

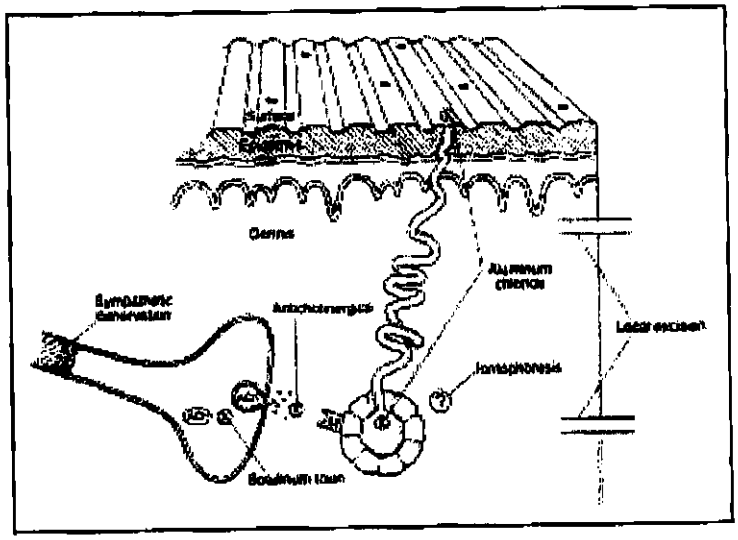

FIGURE 2. A sympathetic sudomotor nerve and an eccrine sweat gland in glabrous skin. Included are the mechanisms of action of the therapeutic modalities for hyperhidrosis (see text). Surgical sympathetic denervation actually is performed more proximally, under video-assisted thoracoscopy, interrupting the corresponding extremity innervation along the thoracic sympathetic chain. The mechanism of action for iontophoresis is unknown. ACh = acetylcholine; M = muscarinic cholinergic receptor.

tion of sweating. A waterproof marker can be used to outline the area, then simple gravimetric analysis is performed on the sweat. This consists of weighing filter paper on a high-precision scale, placing it over the defined region for 60 seconds, then reweighing; thus, the rate of sweat production is defined as milligrams per minute per centimeters squared.[2,31] Dynamic sudorometry using a ventilated capsule method also has been used to quantify sweat output and response to treatment of hyperhidrosis.[32,33]

We use the thermoregulatory sweat test (TST) at our institution both to delineate the distribution of primary hyperhidrosis and to reveal the integrity of skin thermoregulatory sweating in response to a controlled heat and humidity stimulus.[28] The TST at the Mayo Clinic is a modification of the Guttman quinizarin sweat test.[34] Low et al[35] revived the TST by introducing alizarin red indicator to replace quinizarin, the latter often irritating and sensitizing the skin. Fealey et al[28,36] modified Guttman's cabinet so that ambient humidity was regulated and infrared heaters controlled skin temperature. The TST begins with a whole-body skin application of a mixture of alizarin red, cornstarch, and sodium carbonate.[37] The entire anterior body surface and palmar and plantar skin are powdered. Resting (essential) hyperhidrotic areas become evident almost instantly and are photographed (Figure 1). The patient is then placed in a tented heating cabinet where skin and oral temperatures and thermoregulatory sweat recruitment patterns are recorded. Oral (core) temperature is elevated to 38.0°C, at which point all healthy patients sweat profusely, turning the light orange–alizarin red mixture dark purple. The patient is removed from the cabinet and photographed again, and a computer drawing is obtained. The percentages of anhidrosis and hyperhidrosis areas are computer determined from measurements of the different colored regions of body surface area. The distribution of both resting hyperhidrosis and thermoregulatory sweating is obtained, providing an important adjunct in making the diagnosis. Patients with hyperhidrosis typically continue to sweat profusely from the palms and soles while heated, differing from nonhyperhidrotic subjects. Usually all other surface areas sweat normally with a rare patient exhibiting anhidrosis elsewhere. The TST can help confirm and stratify the success and durability of subsequent therapy.

TREATMENT

Anticholinergics and Clonidine

Perhaps unknowingly, early practitioners contributed to the understanding of the mechanism of sweat production by finding that giving elixirs from atropine plants improved this condition.[38] For palmar-plantar hyperhidrosis, systemic anticholinergics such as atropine and glycopyrrolate are seldom used because of adverse effects (eg, sedation, dry mouth, constipation) and the emergence of newer ther-

TABLE 2. **Medications for Hyperhidrosis**

Type of hyperhidrosis	Treatment	Formulation	Route of administration and dosage
Craniofacial, gustatory	Glycopyrrolate	0.5% Solution, cream, or roll-on	Topical, daily; tapered when able
	Clonidine	0.1-mg tablet	Oral, incremental increases up to 0.6-1.2 mg/d in 2 or 3 divided doses
		Transdermal patches, 0.1-0.3 mg/d	0.1 mg/d patch first week; increase weekly up to two 0.3 mg/d patches
Craniofacial, gustatory, menopausal	Bellergal-S	0.3-0.6 mg of ergotamine tartrate, 0.2 mg of belladonna alkaloids, and 40 mg of phenobarbital	One tablet by mouth every 12 h. May need to be compounded by local pharmacy because it is less available than in the past
Axillary, palmar-plantar, craniofacial	Aluminum chloride	20% Aluminum chloride in ethyl alcohol; 12% aluminum chloride in sodium carbonate–water	Topical, nightly, until desired effect is achieved, then taper to once per week; follow *Physicians' Desk Reference* directions carefully for best results
Palmar-plantar, axillary	Iontophoresis unit	Patient-controlled current, 15-30 mA using tap water (from faucet); if this is not effective, glycopyrrolate, 2-mg tablet, can be crushed and added to each water tray	Topical, at each site for 30 min once or twice daily, or 20 min at each site every 2-3 days, or 10 min at each site 3-5 times weekly; the anodo site is most effective so switch sides after half of each treatment

apies. However, for craniofacial hyperhidrosis, medications are currently the most effective therapy (Table 2). Daily application of a topical 0.5% glycopyrrolate solution has been reported to improve craniofacial sweating.[39] The sympathetic inhibitory action of the α_2-adrenergic agonist clonidine has been reported in a patient for whom the dose was increased by increments of 0.05 mg/d until reaching a dose of 0.3 mg/d to 0.4 mg/d, with most of the dose (0.25 mg) taken at bedtime to avoid daytime sedation. As an adjunct, nightly application of 20% aluminum chloride in ethyl alcohol (discussed subsequently) was tapered eventually to every fifth night. By week 3, the patient experienced complete remission with the additional purported benefits of anxiolysis.[40]

Antiperspirants

Over-the-counter antiperspirants contain metal salts, most commonly aluminum chloride, which purportedly blocks the epidermal sweat duct or promotes atrophy and vacuolization of the glandular secretory cells.[41] For more severe cases in which excessive sweat reacts with aluminum chloride to form irritating hydrochloric acid, anhydrous ethyl alcohol added to 20% aluminum chloride hexahydrate is prescribed.[42] The solution must be applied to dry skin, typically before sleep, and washed off 6 to 8 hours later. Effectiveness may be improved by covering the treated area with a T-shirt for axillary application, a shower cap for scalp application, or plastic wrap and overlying gloves or socks for palmar or plantar application, respectively. This should be performed nightly until a desired response is achieved, and frequency of application should be titrated to once or twice per week. Disadvantages include only temporary relief lasting a few days, ineffective relief in severe cases, and cumbersome application. Many patients may have tried this treatment for the hands but may not have followed all the steps just described. In that case, another trial is given with strict adherence to details of the technique, which are clearly described in the *Physicians' Desk Reference* summary page for the drug. This is still the treatment of choice for axillary hyperhidrosis.

Iontophoresis

Since 1984, commercial iontophoresis devices have been available for home use. The mechanism of action is unknown. The battery-powered unit delivers a current through tap water–saturated wool pads, separated by a nonconducting barrier placed directly on the treatment site. Patients increase amperage to the maximum output tolerable and treat each site for 30 minutes, up to twice daily.[43] Patients may require daily treatments for up to 2 weeks, which should decrease sweating for several weeks, and repeat treatments as needed.[43] Adverse effects may include pain and small skin burns from the direct current; therefore, alternating current applicators are being developed.[44] Recently, Dolianitis et al[45] have shown iontophoresis with a 0.05% glycopyrrolate solution to be significantly superior to tap water in suppression of palmar hyperhidrosis. Further development and standardization of the technique and equipment for iontophoresis should substantially enhance this treatment alternative.

Botulinum Toxin

Previously used as an off-label treatment for hyperhidrosis, the US Food and Drug Administration approved the use of botulinum toxin type A (BT-A) for axillary hyperhidrosis in July 2004. Odorless, tasteless, and colorless, botulinum is the most poisonous substance known.[46] Botulinum toxin type A is 1 of 7 types (A-G) of botulinic toxins from the

gram-positive bacillus *Clostridium botulinum*. It was isolated in 1946 in crystalline form and 4 years later was discovered to paralyze a hyperactive muscle on injection.[47] At the sympathetic nerve bouton innervating an eccrine sweat gland, the heavy chain of the BT-A molecule is internalized by receptor-specific endocytosis, and the light chain interferes with a synaptosomal protein, thereby blocking exocytotic release of acetylcholine.[47,48] The longer-lasting inhibition of sweating appears related to BT-A's induced functional denervation of sweat glands, on the basis of immunofluorescence results obtained from growth-associated protein (GAP) 43/protein gene product (PGP) 9.5 stained skin biopsies from patients with palmar hyperhidrosis.[49] Patients can develop antibody titers against BT-A, but this is extremely uncommon with the limited dosing used for palmar or axillary hyperhidrosis.

Botulinum toxin type A is injected intradermally in the affected areas. To reduce the pain of injections, several analgesic therapies have been described, including oral or intravenous sedation medication, topical lidocaine cream, nerve blocks, intravenous regional anesthesia (Bier block), and recently, cryoanalgesia with dichlorotetrafluoroethane.[50] For axillary hyperhidrosis, the BT-A dose is typically 50 to 100 U per axilla, diluted in preserved 0.9% saline. Approximately 20 injections are distributed evenly in the hyperhidrotic area outlined by the Minor starch-iodine test. Sweat reduction should be noticeable in 2 to 4 days and should be substantial within 2 weeks after the first injection.[31,51] Average therapeutic duration is approximately 7 months because sweat function returns gradually over time; subsequent injections are necessary approximately every 4 to 17 months.[51,52]

Disadvantages of BT-A for palmar hyperhidrosis include repeated, uncomfortable injections into the hand that necessitate some form of analgesia or sedation as well as the potential spread of botulinum into the neuromuscular junctions of surrounding muscle beds causing weakness of the thumb–index finger pinch.[53] The risk of intrinsic hand muscle weakness can be minimized by intradermal injection and small-volume reconstitution of BT-A. Nevertheless, a preliminary short-term study has shown that the Dermatology Life Quality Index is significantly improved by BT-A injection in patients with hyperhidrosis of the axillas, palms, or both.[54]

Local Excision

Only applicable for axillary hyperhidrosis, newer techniques of localized surgical removal of eccrine and apocrine sweat glands have gained in popularity since the unsightly or restrictive en bloc excisions were first performed in the 1960s. Both axillary liposuction and curettage, aimed at removing the sweat glands in the dermis-subcutaneous fat junction, can be performed under local anesthesia with use of small incisions, with or without systemic administration of anxiolytics. In general, patients first undergo starch-iodine delineation of the axillary sweat region. After injection of local anesthesia with a vasoconstrictor, a small incision is made, followed by sharp superficial curettage or liposuction. A suction drain may be placed with skin sutures, or the incision may be left open to drain and heal spontaneously, depending on the procedure and the preference of the proceduralist. Significant postoperative improvements in sweating and satisfaction lasting from 6 weeks to 6 months are reported in approximately 80% to 90% of patients.[55-57] Efficacy should be permanent. Disadvantages to the procedure include a potential for scarring, partial alopecia, or hyperpigmentation.[56] Self-limited, short-term adverse effects may include bruising, induration, and pain.[56] Increased operator experience and evolving techniques have substantially improved the appeal of this procedure for axillary hyperhidrosis.

Sympathetic Denervation

After anticholinergics and topical antiperspirants, thoracic chain sympathectomy is the next oldest of the current therapies for palmar hyperhidrosis.[58] Thoracic chain sympathectomy remains successful for long-term therapy for severe palmar hyperhidrosis and, interestingly, for plantar hyperhidrosis, which improves modestly in about 50% to 75% of the patients and in perhaps 80% of patients with coexisting axillary hyperhidrosis.[37] For isolated axillary hyperhidrosis and craniofacial hyperhidrosis, variant techniques are used.

Historically, surgical sympathectomy was reserved for severe cases of palmar hyperhidrosis refractory to the more conservative therapies for several reasons: the invasive nature of the procedure, the need for general endotracheal anesthesia and hospitalization, and perioperative and postoperative complications. Several surgical approaches have been described, evolving to the present minimally invasive video-assisted endoscopic thoracic sympathectomy (ETS), for which 1 small intercostal incision is used for uniportal access in each lateral axilla.

Outcome studies after ETS have received criticism because many end points are subjective and potentially conflict with objective studies. Despite patient satisfaction, TST and starch-iodine test results may reveal partial sweating, sympathetic skin response studies may normalize, and vasomotor studies of cooling and rewarming kinetics also may normalize.[27,37,58,60] For consistency, the term "operative success" typically signifies objective proof of denervation and diminished sweating. In experienced hands, this is greater than 90% and correlates clinically with long-term measurable anhydrosis. The phrase "considered the operation successful" pertains to the patient's subjective satis-

faction in the reduction of original focal sweating. This usually follows objective criteria and is expressed typically in more than 95% of patients but may not correlate with the postoperative degree and area of anhydrosis included in the "operative success" criteria of the postoperative sweat test measurement discussed previously. In fact, dry palms are a satisfying result of modern surgery regardless of how the surgery is performed. "Pleased with overall outcome" combines overall satisfaction with any accompanying adverse effects such as compensatory hyperhidrosis (CH), which typically lower the "overall satisfaction" to approximately 85%.[15,17,27,61-65]

Perioperative complications include the following: life-threatening great vessel injury (extremely rare); hemopneumothorax requiring chest tube placement (1%); and prolonged transient or intercostal neuralgia (1%-2%), which can be minimized with smaller endoscopes and a unipolar approach (J.L.D.A., unpublished data, February 2005). However, unless catastrophic or unusually complicated, perioperative complications typically have a low bearing on the overall patient satisfaction rate. In contrast, cosmetic complications from ETS include Horner syndrome (ipsilateral ptosis, miosis, facial anhydrosis, vasomotor rhinitis) and, most importantly from a patient-satisfaction perspective, an increase in sweating elsewhere on the body (CH). To minimize these complications, much attention has been focused on how, and how much, sympathetic nerve innervation should be interrupted.

Once it was determined that the second thoracic sympathetic ganglion was the largest physiological relay center to the upper extremity,[66] surgical therapy for hyperhidrosis has included vigilant avoidance of damage to the stellate ganglia (Figure 3). Before the 1940s, Horner syndrome resulted from surgery because the stellate ganglion was removed.[58] With endoscopic visibility, the 5% complication rate for Horner syndrome from older supraclavicular or posterior thoracic surgical approaches has been lowered to 1% to 2%.[15,17,27,61-65] Only in severe cases of craniofacial hyperhidrosis is stellate ganglionectomy considered, and this occurs after the patient has undergone a preoperative stellate nerve block to accept the cosmetic sequelae of Horner syndrome. The variant operation for isolated axillary hyperhidrosis generally involves sympathetic chain ablation inclusive of more sympathetic chain segments, starting at T2 or T3, and ablation of each segment caudally to approximately T4.[62]

Compensatory hyperhidrosis is by far the most common and disagreeable complication of sympathectomy, producing subjective and objectively measurable increased sweating in body segments usually just below the areas made dry by sympathectomy. With traditional sympathectomies or ganglionectomies (Figure 3), severe CH may occur in 10%

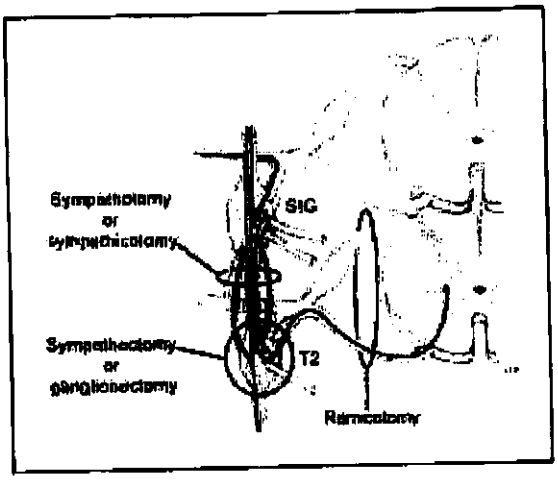

FIGURE 3. The sympathetic chain and the various targets of surgical sympathetic denervation. Preganglionic sympathetic nerves (including audomotor nerves) exit the spinal cord from segments T1 to L2-3 and course up and down the paravertebral sympathetic chain to innervate postganglionic nerves. Often, the inferior cervical ganglion is fused with the first thoracic ganglion, called the stellate ganglion (StG), which must be spared to minimize the risk of postoperative Horner syndrome (see text). Ganglion-sparing endoscopic thoracic sympathotomy is restricted to electrocauterization of the chain between the stellate and T2 ganglion, minimizing the risk of severe postoperative compensatory hyperhidrosis in other regions of the body.

to 40% of postoperative patients.[37] It is interesting that the sites affected with CH are generally the thermoregulatory, nonglabrous skin regions of the trunk/back, buttocks, groin, and thighs that sweat normally before ETS. A plausible explanation is that CH results from more aggressive procedures targeting resection of several ganglia, intervening chain, or white rami communicantes and their axons from cells in the intermediolateral cell column of the spinal cord. Henceforth, large areas of anhidrosis occur with increased severity of CH, such that normal thermoregulatory effectors become up-regulated as a mechanism of normal heat dissipation.[67] This may lead ultimately to long-term debilitating CH with few treatment options, and at least 5% of patients may regret undergoing the operation.[65]

Typical surgical sympathectomies for palmar hyperhidrosis have consisted of excision or electrocautery ablation of the T2 and/or T3 sympathetic ganglion. Recently, our institution modified this technique by preserving the ganglia and performing a simple chain disconnection between the T2 ganglion and the stellate ganglion (Figure 3). Termed *sympathotomy*, this procedure produces excellent results and clinically diminishes the chances of severe CH.[37] Termed *sympathicotomy* in other countries, this technique and the disconnection of sympathetic rami (*rami-*

cotomy) will require further long-term investigation of the postoperative risk of severe CH.

Intraoperative predictability of successful outcome depends on monitoring of the acute response to surgical denervation and abrupt release of sympathetic tone. These modalities include assessment of instantaneous skin blood flow changes with laser-Doppler flowmetry and increases in fingertip or palmar skin temperature. Importantly, the average intraoperative fingertip temperature increase of 1.2°C with sympathotomy in our experience is lower than the skin temperature increase of about 3°C reported with more destructive procedures.[68] This has important implications in the choice of intraoperative monitoring techniques because smaller changes in temperature, when considered alone, may raise doubt about the procedure's therapeutic efficacy. Therefore, we routinely monitor skin blood flow with laser-Doppler for real-time surgical feedback, serving as an adjunct to fingertip temperature, which lags by 3 to 5 minutes.[68]

Information on the long-term physiological sequelae is emerging rapidly. Preoperatively, in addition to abnormal sudomotor control, sympathetic cardiovascular regulation may be affected mildly in severe cases of hyperhidrosis. A blunted reflex bradycardia response to parasympathomimetic maneuvers such as Valsalva maneuver or cold water face immersion, as well as an increased heart rate response to orthostatic stress, suggests a hyperfunctioning sympathetic discharge that is reversed after ETS.[21,69] Because sympathetic cardiac accelerator fibers exit the spinal cord from segments T1 to T4, ETS is believed to simulate a mild physiological β-adrenergic blockade.[70] This is because the heart rate at rest and during maximal exercise is lower 6 weeks postoperatively,[69,71] but exercise capacity is not affected. As for pulmonary sympathetic denervation, no significant detrimental effect on pulmonary function has been shown in children and adults.[72] The return of vasomotor function[27,73] has rendered ETS less desirable for conditions such as Raynaud phenomenon and chronic regional pain syndrome.

Cost

The costs of surgical treatment of hyperhidrosis considerably exceed those of nonsurgical treatment. These initial differences may be attenuated with time, if the need for long-term treatment in nonsurgical patients is factored in. Cost differences also may be related to the success of treatment in individual patients, the experience of the health care clinicians, the regional differences in overall health care costs, and the methods of reimbursement. Potential differences in costs with these evolving treatments can be estimated most accurately if the sponsoring physician first assesses the extent of the patient's disease and the individual patient or physician questions the clinicians most likely to care for the patient.

SUMMARY

One of the oldest described dermatologic conditions, primary hyperhidrosis is an embarrassing disorder that, even today, is misconceived as rare and untreatable. It is exacerbated during emotional stress, and the pathophysiological mechanism appears to be hyperfunctioning efferent sudomotor outflow, controlled by the anterior cingulate cortex. Primary hyperhidrosis is associated with few or minimal autonomic comorbidities. Treatments are based on the severity of sweating intertwined with the risks and benefits of each modality. Increased medicosocial awareness and evolving therapies are improving the efficacy of treatment and minimizing adverse effects. For more information, patients can be referred to the International Hyperhidrosis Society (www.sweathelp.org), a nonprofit global organization that provides education, advocacy, access to hyperhidrosis treatment, and research into excessive sweating.

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Questions About Hyperhidrosis

1. Which *one* of the following statements about hyperhidrosis is *false*?
   a. It can be a heritable disorder in 25% to 50% of cases
   b. It affects adolescents of any ethnic background
   c. It is bothersome during sleep
   d. The pathophysiological mechanism is unclear
   e. The prevalence approaches 2.8% of the US population
2. Which *one* of the following statements about the diagnosis of primary hyperhidrosis is *false*?
   a. The history and physical examination have more bearing than laboratory studies in making the diagnosis
   b. Numerous autonomic abnormalities coexist with hyperhidrosis
   c. Long-term exposure to pesticides or biochemical agents may mimic primary hyperhidrosis
   d. Patients will describe symptom exacerbation during stressful situations
   e. It must be differentiated from secondary hyperhidrosis
3. Which *one* of the following would *not* present similar to hyperhidrosis?
   a. Thyrotoxicosis
   b. Chronic lymphocytic leukemia
   c. Tuberculosis
   d. Menopause
   e. Pure autonomic failure
4. Which *one* of the following treatments is extremely *effective* against axillary hyperhidrosis and recently received Food and Drug Administration approval?
   a. BT-A injections
   b. Oral glycopyrrolate
   c. Local surgical curettage
   d. Surgical sympathectomy
   e. Aluminum chloride salts
5. Which *one* of the following surgical objectives attempts to minimize severe postoperative CH?
   a. Stellate ganglion excision
   b. Minimally invasive sympathetic chain disruption
   c. Sympathetic chain disconnection at several levels
   d. Open thoracotomy procedure with multiple ganglion excisions
   e. No method of minimizing this complication exists

Correct answers:
1. *c*, 2. *b*, 3. *e*, 4. *a*, 5. *b*

ORIGINAL ARTICLE

Endoscopic Transthoracic Limited Sympathotomy for Palmar-Plantar Hyperhidrosis: Outcomes and Complications During a 10-Year Period

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OBJECTIVE: To review surgical results of endoscopic transthoracic limited sympathotomy for palmar-plantar hyperhidrosis during the past decade.

PATIENTS AND METHODS: We retrospectively reviewed 155 consecutive patients who underwent surgery from June 30, 2000, through December 31, 2009, for medically refractory palmar-plantar hyperhidrosis using a technique of T1-T2 sympathotomy disconnection, designed for successful palmar response and minimization of complications.

RESULTS: Of the 155 patients, 44 (28.4%) were male, and 111 (71.6%) were female; operative times averaged 38 minutes. No patient experienced Horner syndrome, intercostal neuralgia, or pneumothorax. The only surgical complication was hemothorax in 2 patients (1.3%); in 1 patient, it occurred immediately postoperatively and in the other patient, 10 days postoperatively; treatment in both patients was successful. All 155 patients had successful (warm and dry) palmar responses at discharge. Long-term follow-up (>3 months; mean, 40.2 months) was obtained for 148 patients (95.5%) with the following responses to surgery: 96.6% of patients experienced successful control of palmar sweating; 69.2% of patients experienced decreased axillary sweating; and 39.8% of patients experienced decreased plantar sweating. At follow-up, 5 patients had palmar sweating (3 patients, <3 months; 1 patient, 10-12 months; 1 patient, 16-18 months). Compensatory hyperhidrosis did not occur in 47 patients (31.7%); it was mild in 92 patients (62.2%), moderate in 7 patients (4.7%), and severe in 2 patients (1.3%).

CONCLUSION: In this series, a small-diameter uniportal approach has eliminated intercostal neuralgia. Selecting a T1-T2 sympathotomy yields an excellent palmar response, with a very low severe compensatory hyperhidrosis complication rate. The low failure rate was noted during 18 months of follow-up and suggests that longer follow-up is necessary in these patients.

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rH = relative humidity; TST = thermoregulatory sweat test

Sympathetic nervous system surgery for hyperhidrosis has been practiced by the Mayo Clinic Department of Neurosurgery for more than 75 years.[1] The palmar component of palmar-plantar hyperhidrosis has always been the target of thoracic surgery, with less predictable beneficial results for the axillae and feet. Endoscopic transthoracic approaches were introduced by Kux[2] in 1951, and with improved optics and light sources, this approach has been used in virtually every hyperhidrosis surgical series for the past 20 years. Uniportal approaches are possible with improved optics when performed by experienced surgeons.[3] Although the transthoracic endoscopic approach is currently practiced at all medical centers, the operation devised to interrupt the sympathetic flow to the hands varies considerably: resection, ablation, clips, and cautery have all been applied to various regions of the upper sympathetic thoracic chain.[4-9] Life-threatening complications are rare with the endoscopic transthoracic approach, regardless of how the sympathetic chain is operated. Because there is no uniformly agreed on approach for interruption of the sympathetic chain (the actual operation for this condition), rates of success and risks of complication vary. However, recent series strongly suggest what we have practiced for more than a decade: simple T2 sympathectomy yields excellent results for the hands and lessens the chances of severe postoperative compensatory hyperhidrosis, and the more aggressive resections of the sympathetic chain increase the risk of severe postoperative compensatory hyperhidrosis.[10-16] The extremely disagreeable complication of severe compensatory hyperhidrosis (in which the patient regrets the operation because of resultant profound increased new sweating elsewhere) remains the most problematic because no satisfactory treatment is available if it occurs.

For editorial comment, see page 717

We designed our operative approach to render a high success rate in the treatment of severe palmar hyperhidrosis and minimize possible complications (which we previously described[17,18]) by initiating the following strategies.

1. *Maximize Palmar Response to Surgery.* We designed the surgical procedure to effectively eliminate any sympathetic output to the brachial plexus in the hand, except through the T1 ganglion (or C8 and T1 fusion, the stellate ganglion) by disconnecting all sympathetic connections below this level (T2 sympathotomy). Others have found excellent results using this technique as well.[10,11] We added an intraoperative laser Doppler palmar blood flow monitoring machine (PeriFlux System 5000; Perimed AB,

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Järfäll, Sweden) and computer analysis. The system injects laser light into tissue through Doppler probes adhered to the palmar aspect of each thumb and measures wavelength alterations caused by flowing blood. This provides real-time feedback of completed loss of sympathetic tone to the hand, and this approach is markedly more effective than relying on fingertip temperature changes alone.[19] The operation is anatomically completed when all visualized sympathetic branches between the T1 ganglion and the T2 ganglion have been severed across the second rib, and it is physiologically confirmed by an instantaneous increase in palmar blood flow when the loss of sympathetic tone is complete.

2. *Minimize Intercostal Neuralgia.* This painful thoracic nerve injury is due to instrumental pressure on the intercostal nerve in the narrow confines between the ribs; it occurs in 2% to 3% of endoscopic transthoracic procedures, and in severe cases, the injured intercostal nerve may emanate pain for months or even years.[4-9,13,14] We designed a very small single-incision, uniportal trochar approach, using a straight lens 3-mm Gaab endoscope, engineered at Mayo Clinic, to couple with a sleeve-attached monopolar cautery matching the focal point of the lens, to minimize thoracic nerve irritation between the ribs by minimizing the whole operating instrument to smaller than the width of a pencil (Figure 1). The diameter of the device allows placement through the intercostal approach without compressing the intercostal nerve and does not compromise optical visualization.

3. *Minimize Severe Compensatory Hyperhidrosis.* Mild increased sweating occurs postoperatively in new compensatory areas in a large percentage of patients, regardless of how the procedure is performed. However, *severe compensatory hyperhidrosis* is generally an accepted term when a patient develops new areas of increased sweating postoperatively that are so severe the patient regrets having undergone the procedure. In most series in which sympathectomy (removal of the sympathetic chain) has been performed, the unpredictable complication of severe compensatory hyperhidrosis occurs in 5% to 20% of patients.[4-9,13,14] We designed our surgical approach to minimize this complication on the basis of evidence that the more destructive the procedure, the higher the risk of postoperative severe compensatory hyperhidrosis.[9-15] Therefore, we perform only a limited, single-level sympathotomy and do not remove any of the sympathetic chain (sympathectomy). All branches and connections to the brachial plexus across the second rib are disconnected, isolating the T1 (or stellate) ganglion as the only input to the hand and ensuring that ganglion cells in T1 and T2 remain undisturbed (Figure 2). These ganglia may be important if injured because axons from the spinal cord to the ganglia would necessarily be injured as well, which could theoretically cause synaptic reorganization of spinal cord sympathetic reflexes and may increase the risk of severe compensatory hyperhidrosis. In essence, the procedure is the least invasive that can be performed to ensure success of the surgery and minimize complications.

The aforementioned information serves as background. The purpose of this report was to review surgical results of endoscopic transthoracic limited sympathotomy for palmar-plantar hyperhidrosis during the past decade.

PATIENTS AND METHODS

We retrospectively reviewed 155 consecutive patients with medically refractory palmar-plantar hyperhidrosis who underwent surgery in the Mayo Clinic Department of Neurosurgery from June 30, 2000, through December 31, 2009. The Mayo Clinic Institutional Review Board approved the study, and no patient was contacted for follow-up against his or her wishes. Preoperatively, a variety of oral agents, topical agents, and in many cases tap water iontophoresis had failed in all patients, and all were judged to have severe refractory palmar-plantar hyperhidrosis. Some patients had received off-label use of botulinum toxin injections to the hands. Importantly, patients with hyperhidrosis that predominantly affected the axillae or patients with primarily a craniofacial hyperhidrosis were not deemed surgical candidates. All patients were preoperatively assessed outside the Department of Neurosurgery by the department of neurology, dermatology, or pediatrics and referred for surgical consideration after noted failure of medical strategies. All patients had a confirmatory history, had undergone a physical examination, and had undergone thermoregulatory sweat testing (TST) and were observed to have beading or drippage of sweat from palms during physical examination or in the thermoregulatory laboratory before heat exposure. The TST, using indicator powder, provided visual confirmation of the preheat, resting sweat distribution, and the heat-stimulus portion of the TST ruled out compensatory palmar sweating due to anhidrosis elsewhere. Later in the series, quantitative emotional sweat output was obtained (Figures 3 and 4). A ventilated capsule containing a calibrated humidity sensor was fashioned, and a recording was made simultaneously from both palms and the left forearm. Such data have been advocated to objectively quantitate the severity of a patient's hyperhidrosis and stratify treatment options on the basis of severity.[20]

Attempts were made to contact all patients postoperatively for follow-up by outpatient consultation, telephone interview, or questionnaire and written correspondence. The 155 patients consisted of 111 females (71.6%) and 44 males (28.4%). The median age for females was 22 years

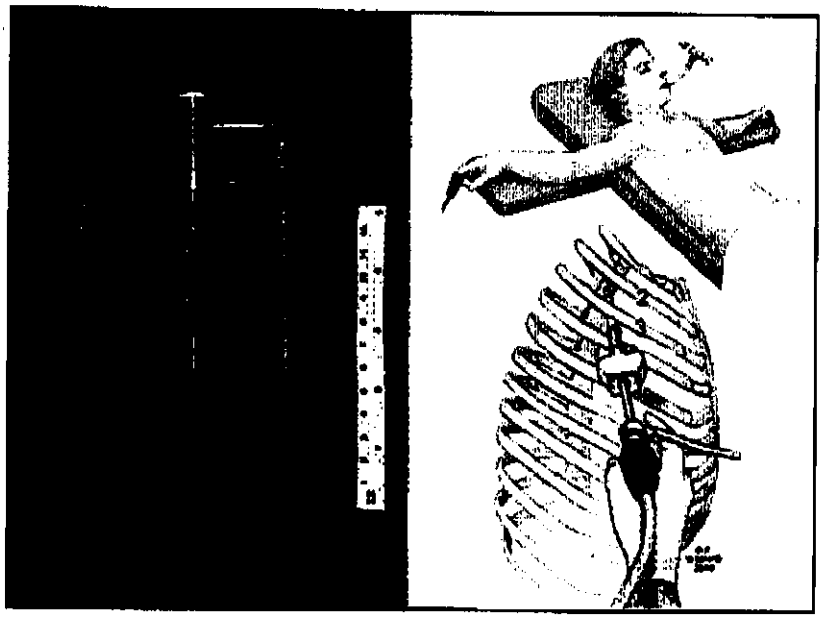

FIGURE 1. Left, Hollow trochar with obturator (first object) for perforating chest wall allows penetration of the chest wall through a small (<1 cm) incision, removal of the inner obturator, and passage of the Gaab straight lens endoscope with engineered attached monopolar cautery probe (second object). Pencil and tape measure provide perspectives of size. The Mayo engineered hollow trochar with blunt perforating obturator removed mates perfectly with the engineered endoscope/cautery unit. Right: upper, Position of patient at surgery; lower, Single small incision and uniportal access with endoscope and cautery combined.

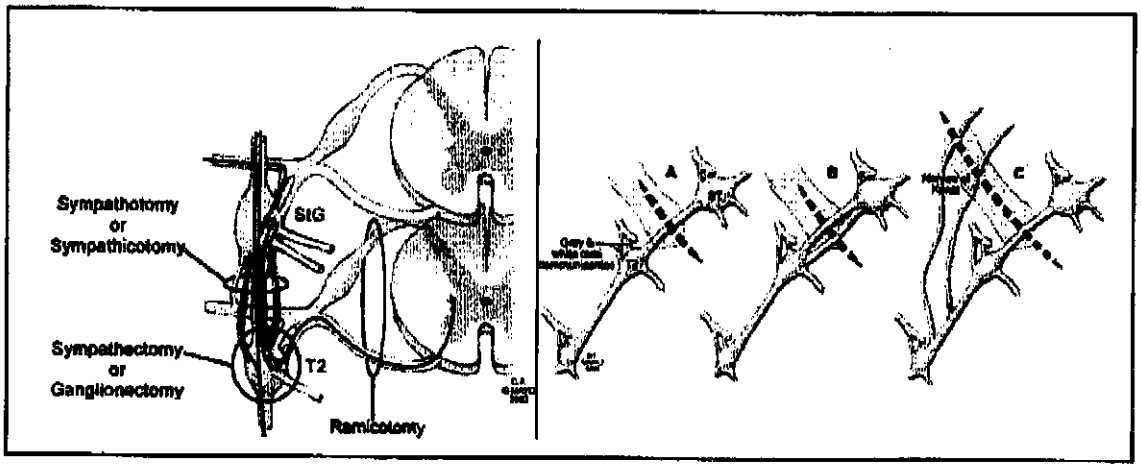

FIGURE 2. Left, Schematic drawing of sympathectomy vs sympathotomy. Note that sympathectomy, with use of ganglionectomy by definition, must sever the primary axon from the neuron in the intermediolateral cell column of the spinal cord (red) before primary or collateral synapse in the T2 ganglion. This injures the neurons at this level of the spinal cord, some of which may die, and may predispose the patient to spinal cord neuronal synaptic reorganization and severe compensatory hyperhidrosis. Sympathotomy interrupts only axons after potential T2 ganglion synapses, a less injurious effect on the neuron, and is the least destructive procedure possible for successful treatment of palmar hyperhidrosis. StG = stellate ganglion. Right, All sympathetic connections across the second rib between the StG and the T2 ganglion are severed. (A) depicts a single trunk, (B) multiple trunks (6 patients), (C) trunk with lateral nerves of Kuntz (16 patients). Severing all sympathetic innervation across the second rib between the StG and T2 ganglion ensures that only the StG can provide sympathetic outflow to the hand through the brachial plexus, and this strategy minimizes axonal injury at the spinal cord level (left panel).

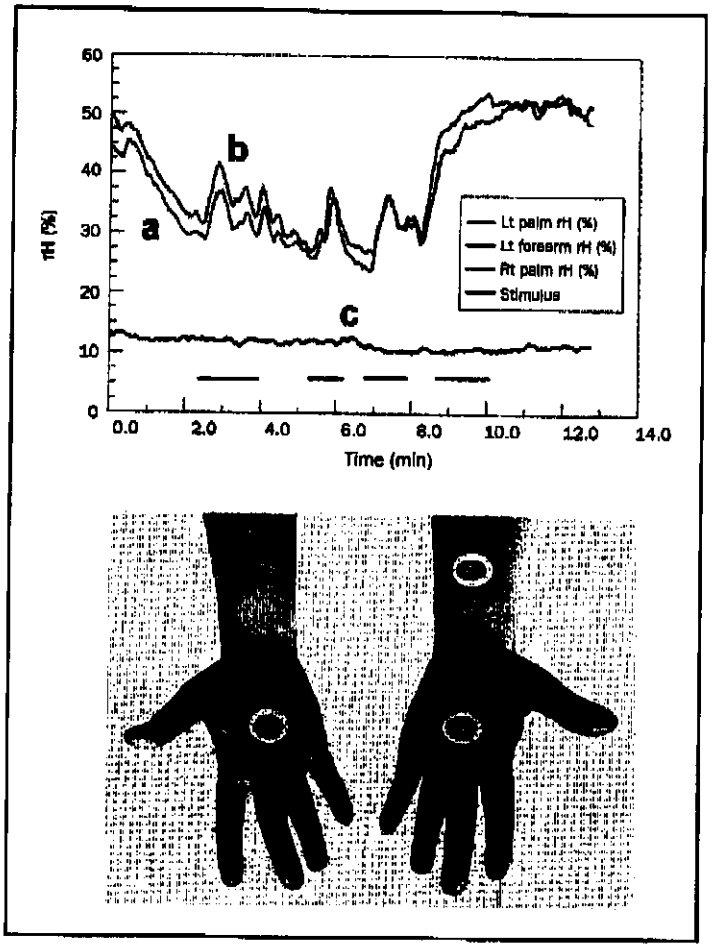

FIGURE 3. Two ways of assessing palmar hyperhidrosis. Upper, Ventilated capsule measurements capture the detailed synchronous pulsatile and localized palmar (a and b traces) sweat output with emotional stimuli. Lt = left; rH = relative humidity; Rt = right. Lower, in same patient, the resting sweat produces a purple discoloration of the alizarin red indicator powder in palms but not the forearm. Lettered ovals refer to capsule locations.

and for males, 23 years; 25 females (22.5%) and 15 males (34.0%) were 18 years of age or younger. Family history was positive in 84 patients (54.2%). Onset of symptoms occurred at the following ages: 0 to 3 years old in 42 patients (27.1%); 4 to 8 years old in 74 patients (47.7%); 9 to 12 years old in 29 patients (18.7%); and greater than12 years old in 10 patients (6.5%).

Operation

At arrival of the patient to the operating room, general anesthesia was induced in the supine position, followed by placement of a double-lumen endotracheal tube for intermittent one-lung ventilation. Then, both arms were abducted to 90°, and the back was elevated to 40°. After sterile skin preparation and draping, the chest wall was perforated through a 1-cm or less skin incision with a small blunt obturator and hollow trochar, engineered for perfect passage of the small endoscope and attached monopolar cautery unit. Gravity was used to descend the lung a few centimeters from the apex to perform the procedure because there is no pressurized gas insufflation with this technique (Figure 1). We performed the procedure (described subsequently) on the right side first; once the procedure was completed, a pediatric feeding tube was inserted to serve as a vent for retained air, and the right lung was ventilated. We then performed the identical procedure on the left side, again inserting a pediatric feeding tube and ventilating both lungs. The wounds were closed,

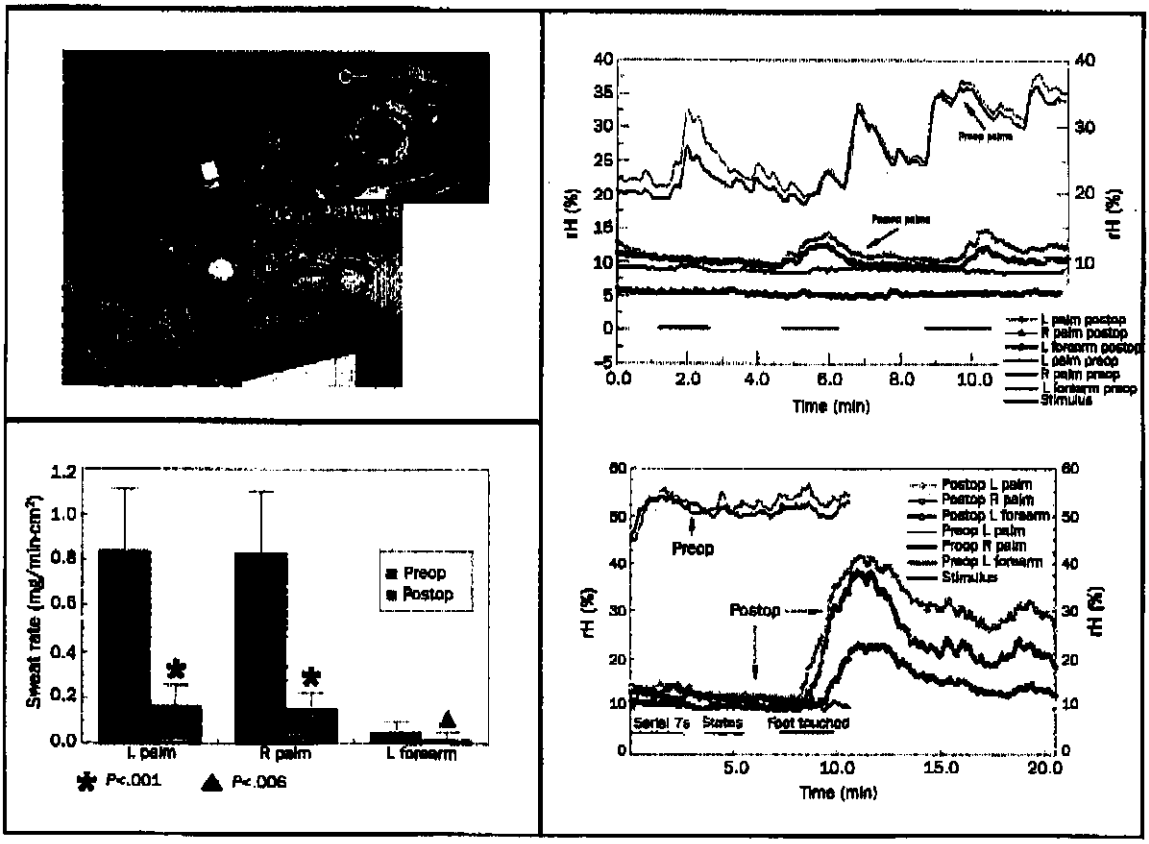

FIGURE 4. Linear relationship between mean measured relative humidity (rH) and normalized sweat rate. Top left, Ventilated capsule setup for recording quantitative palmar and left (L) forearm sweat rates. Inset: A, The HIH 3610 (humidity sensor; Honeywell Sensing and Control, Golden Valley, MN); B, thermistor probe to measure skin temperature; and C, desiccated air tubing connecting to capsule. All 3 capsule sites are plotted. Clustering of responses below 10% rH relates to low sweat rates in the forearm site. Lower left, Quantitative sweat output in patients studied before and after upper thoracic endoscopic sympathotomy. Mann-Whitney U test reveals highly significant reductions in sweat rate for both palms and less robust reduction in forearm. Preop = preoperatively; Postop = postoperatively. Lower right, Surprising palmar and forearm emotional sweat outburst in patient postop. Marked reduction in resting sweat was noted postop with serial 7 and naming states stimuli (from 0-5 minutes); however, when examiner touched patient's feet (7.5-10 minutes), a remarkable sweating response was noted in palms and L forearm postop. R = right. Upper right, Mild emotional-induced sweating is often detected postop but is usually unnoticed by the patient.

and the intrapleural air was aspirated through the bilateral pediatric feeding tubes, which were then removed. Chest radiography confirmed postoperative obliteration or minimal intrapleural air remaining postoperatively. In general, for comfort measures, patients were discharged after a 23-hour observation period, although occasional patients were discharged the same day.

Sympathotomy was performed in all patients by cautery disconnection of the sympathetic trunk and all visible branches above the T2 ganglion and below the T1 ganglion (or stellate) across the second rib. No ganglia were violated anatomically on the basis of correct anatomic location and endoscopic visualization. A minimal (generally ≤1 cm) transaxillary incision was performed in 150 patients, and 5 patients underwent an anterior midclavicular approach between the second and third ribs by uniportal access (≤1-cm incision) because of the size of the chest cavity or body mass index limiting an axillary approach. The Gaab straight lens endoscope with Mayo engineered coapted insulated monopolar cautery probe (Figure 1) was used, and the laser Doppler palmar blood flow device was instituted to ensure physiologic response of the sympathotomy in all but the first 12 patients (143 patients). Blood flow elevation without fluctuations during further ipsilateral cautery or contralateral stimulation ensured physiologic removal of sympathetic tone to the vasculature of the operated hand. This provided a markedly improved real-time feedback during severance

TABLE 1. **Operative Data for 155 Patients Who Underwent Sympathotomy for Palmar-Plantar Hyperhidrosis**

Operative times	Average, 38 min (from skin incision on one side to skin closure on contralateral side)
Sympathetic yoking	11 patients (significant contralateral laser Doppler blood flow changes during surgery on ipsilateral side)
Reinsertion side	2 patients (reinsertion on the initial right surgical side after contralateral left stimulation revealed vasoconstriction, suggesting the initial right surgical side still harbored anatomic sympathetic input)
Nerves of Kuntz	16 patients, 21 sides (6 right, 5 left, 5 both)
Multiple sympathetic trunks	6 patients (all left-sided; 2 trunks in 3 patients; 3 trunks in 3 patients)
Complications	Hemothorax in 2 patients (occurred immediately in 1 patient and 10 d postoperatively in the other patient)

of sympathetic tone to the hand, over and above fingertip temperature probes alone.

The following describes the procedure, which is presented in the supplementary narrated video (see Supporting Online Material, a link to which is provided at the end of this article). The skin blood flow monitor is displayed as a "picture-in-picture" overlay on the surgical videoscope monitors. After the probes are secured to the palm on each hand of the patient simultaneously, a cutaneous temperature probe is also placed on both index fingertips. The operation is performed on the right side first. The right lung is nonventilated to allow visualization of the sympathetic chain. As the electrocautery probe moves across the chain overlying the second rib, marked increases in ipsilateral skin blood flow are nearly instantaneous. On the left palm, the skin blood flow is reduced because of the normal sympathetically mediated vasoconstrictor response to surgical stimulation. When the procedure is performed on the left side, separation of the left sympathetic chain evokes an increase in skin blood flow on the left side. Importantly, as the electrocautery probe courses along the left chain, profound vasodilation is present on both sides that is no longer reactive to any surgical or sympathetic stimulation. This confirms bilateral sympathotomy and predicts a more successful outcome in patients with hyperhidrosis than fingertip temperature alone.

Operative times from skin incision on one side to skin closure on the contralateral side (completed surgery on both sides) averaged 38 minutes. In 2 patients, the operative site was reopened on the initial right side, and further cautery performed after surgery on the left side revealed laser blood flow changes on the right side, suggesting that sympathetic tone was still present. The sympathotomy was completed in these 2 patients by further cautery, which produced a marked rise in measured palmar blood flow concomitant with an absence of further reactivity in Doppler blood flow. Interestingly, 11 patients exhibited significant yoking of the sympathetic response, presumably through spinal cord reflexes, with dramatic increases in blood flow on the contralateral side after the initial right-sided sympathotomy, which further increased after completion of sympathotomy on the contralateral side. Nerves of Kuntz[21,22] were identified in 16 patients (10%), on 21 sides (6 on the right, 5 on the left, and 5 on both sides). More than 1 visible trunk was identified in 6 patients, and all were on the left side (2 trunks in 3 patients; 3 trunks in 3 patients) (Figure 2). Operative information is summarized in Table 1.

RESULTS

All 155 patients had dry hands immediately postoperatively and during hospitalization.

No patient experienced Horner syndrome, intercostal neuralgias perioperatively or in long-term follow-up, or pneumothorax. Two patients experienced hemothorax and required treatment. In the one patient, the hemothorax was immediate; a chest tube was inserted, atelectasis occurred subsequently, and the patient was hospitalized for 6 days but had an uneventful discharge. The other patient returned 10 days after surgery with increasing shortness of breath; chest radiography revealed a moderate left-sided hemothorax. The patient was hospitalized for 3 days and underwent chest tube placement, followed by successful thoracentesis and irrigation removal of a liquefied hematoma.

All patients were advised preoperatively that long-term follow-up was necessary. Patients were contacted and assessed by return evaluations, telephone interviews, or questionnaires. No follow-up was obtained beyond the day of discharge for 2 patients. In 5 patients, follow-up was less than 3 months (on the basis of short-term follow-up of these patients, the procedure was successful. It is highly probable that, if the procedure had failed in any of these 7 patients, the surgical team would have been contacted. Figure 5 summarizes the 2-year follow-up and all documented surgical failures, with Kaplan-Meier estimates for the total surgical group of 155 patients.

Excluding the 7 patients with short-term follow-up, follow-up of the remaining 148 patients (95%) ranged from 3 months to 120 months, with a median of 34 months and mean of 40.2 months. The surgical outcomes of patients with follow-up greater than 3 months are discussed subsequently.

The palmar response to sympathotomy was considered successful by the patient in 143 patients (96.6%); 128 patients (86.5%) considered their hands very dry or with no or minimal sweating, and 15 patients (10.1%) considered the operation highly successful, and their hands exhibited

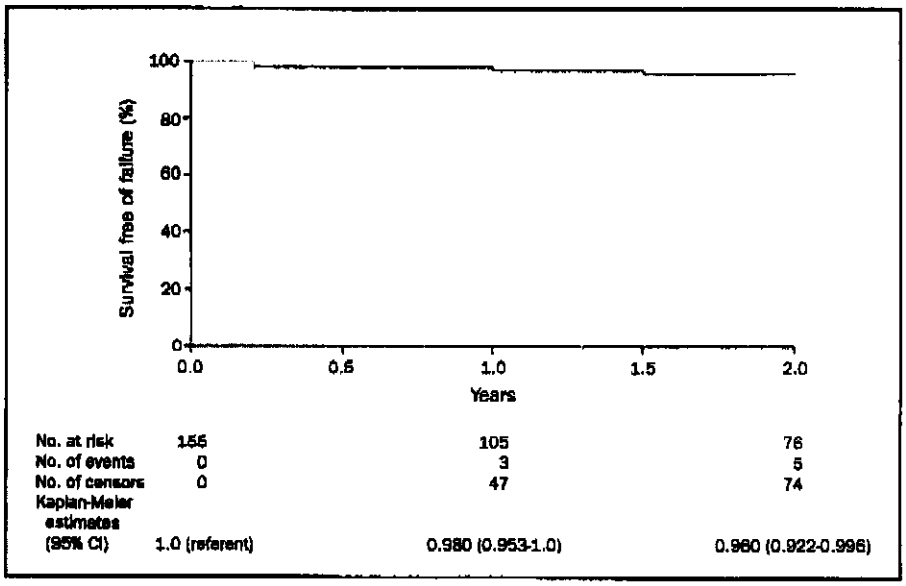

FIGURE 5. Kaplan-Meier estimated survival free of surgical failure in 155 patients. Five of these patients had documented surgical failure, all within 2 years postoperatively. The median length of follow-up after surgery in the remaining 150 patients was 2.1 years; range, 1 day to 9.9 years. CI = confidence interval.

normal heat- or exercise-induced sweating, but with none of the anxiety- or emotional-induced sweating that was present before surgery. Of the 143 patients with successful palmar response to sympathotomy, 99 patients (69.2%) had dryer armpits, whereas 44 (30.8%) had no change; 57 patients (39.8%) had dryer feet, 84 (58.7%) had no change, and 2 (1.3%) had increased sweating of their feet. Results for the axillae and feet are patient responses to questions whether or not these areas had excessive hyperhidrosis preoperatively.

Fifty patients (32%) underwent preoperative quantitative measurement of palmar and left forearm sweating rate via a calibrated ventilated capsule technique. The capsule components and placement are shown in Figure 4, upper left. Capsules were ventilated with dried air at 0.2 L/min. After a 2-minute stabilization period, the percent baseline relative humidity (rH) was obtained. This was followed by a 12-minute observation period during which each patient was subjected to emotional stimuli, including performing serial 7 calculations, timed recitation of US state names, and touching of their feet by the examiner. Capsule percent rH was measured in real time and used to calculate the normalized sweat rate. A linear relationship between mean percent rH and the cumulative sweat rate in milligrams/minute per centimeter squared was found. Sweat rates of the forearm remained near baseline, whereas palmar sweat rates ranged from 0.25 to 0.50 for mild, 0.5 to 0.75 for moderate, and above 0.75 mg/min-cm^2 for severe (beading or sweat drippage visible) palmar sweating. A patient who had severe sweating is shown in Figure 3.

Sixteen patients (10%) were studied at a mean of 4 months postoperatively, and the palmar and forearm sweat rates preoperatively and postoperatively are shown in Figure 4, lower left. For this smaller subset, the preoperative vs postoperative sweat rate at each site was compared using the Mann-Whitney U test. The postoperative sweat rate reduction was significant for all sites, especially for the palms (P<.001): preoperative palmar sweat rate for left (0.840±0.27 mg/min-cm^2) and right (0.830±0.27 mg/min-cm^2) compared with postoperative palmar sweat rates for left (0.166±0.09 mg/min-cm^2) and right (0.153±0.07 mg/min-cm^2). Preoperative left forearm sweat rate was 0.050±0.04 mg/min-cm^2, and postoperative, 0.018±0.03 mg/min-cm^2 (P<.006). Postoperative palmar sweat rates were still greater than preoperative forearm sweat rates in most patients, and occasionally, emotional palmar sweat outbursts occurred (Figure 4, lower right). The cause of this residual sweating is speculated to be the result of nerve regeneration through the stellate ganglia, increased neural traffic through existing pathways from the stellate, denervation supersensitivity of adrenergic or cholinergic receptors, or reorganization and up-regulation of the density of sweat glands.[23] These speculative mechanisms may also explain the 5 bilateral palmar hyperhidrosis failures; 3 patients experienced failure within 3 months postoperatively; 1 patient between 10 months and 12 months; and

1 patient between 16 and 18 months postoperatively. Two patients had mild increased compensatory hyperhidrosis on the trunk and thighs but did not seek postoperative treatment; the 3 other patients in whom surgery failed had no increased sweating elsewhere. Additionally, these 5 patients did not have decreased sweating in their axillary and plantar components. Thus, all 5 patient failures, with recurrence of palmar hyperhidrosis, reported absent or only mild new compensatory sweating.

Compensatory hyperhidrosis was graded as none (patient develops no new sweating elsewhere); mild (patient develops new mild sweating in other areas, but it does not bother patient); moderate (patient develops new sweating in other areas to the degree that patient desires treatment); and severe (patient develops new sweating so severe that patient regrets undergoing the procedure). New areas of increased sweating were most commonly described on the low back, abdomen, buttocks, and thighs, and all long-term follow-up patients are included, whether the procedure was a success (143 patients) or a failure (5 patients). Our compensatory hyperhidrosis results are as follows: no increased sweating in 47 patients (31.7%); mild increased sweating in 92 patients (62.2%); moderate increased sweating in 7 patients (4.7%); and severe increased sweating in 2 patients (1.3%). Interestingly, the 2 patients with severe compensatory hyperhidrosis who regretted undergoing the procedure had very dry hands and no new increased sweating in a temperature-controlled environment, but they had a profoundly increased sweating response to environmental heat or exercise, which is why they regretted undergoing the procedure. Three patients had increased sweating in presurgical areas already involved with hyperhidrosis: 1 patient with a mild increase in gustatory sweating, and 2 patients with mild increased sweating in their feet.

The effect of sympathotomy on cardiovascular function has been previously published in a subset of patients from this series. Results suggest that the sympathotomy procedure used at Mayo Clinic causes detectable changes in cardiovascular control, but this likely has minimal clinical or quality-of-life consequences.

DISCUSSION

The sympathotomy operation performed at our institution divides all branches of the sympathetic chain (separate trunks and nerves of Kuntz) across the second rib between the T1 and T2 ganglia. The operation intentionally does not remove or injure ganglia of the chain or axons from spinal cord neurons innervating the ganglia. As a result, this approach decreases synaptic reorganization at the sympathetic chain level, as well as at the spinal cord level. The operation was designed to shorten operative time, to facilitate a high degree of success for the palmar component of this condition, and to minimize all possible complications, especially severe compensatory hyperhidrosis. The 0% rate of intercostal neuralgia and Horner syndrome is lower than that in reported series, and the 1.3% rate of chest tube for hemothorax is at the lower end of the reported complication range of 1.35% to 5%.[5-7,10,11] The high success rate and very low severe compensatory hyperhidrosis rate demonstrated in this large series of patients prove the validity of this approach, suggesting that a more uniform technique could be considered by other surgeons as well. Also, by adopting a very small incision uniportal access and using a smaller endoscope, we have shortened total surgical time to an average of 38 minutes, and no intercostal neuralgia complications occurred.

The limitations of the current study are that it is a retrospective analysis and subject to the biases of patient responses. Despite every effort to stay in touch with these patients, most are young, mobile, and sometimes difficult to locate. Only 2 patients regretted undergoing the procedure, which is as low or lower than that reported in other series. We found no discernible difference in success or failure of the procedure with patient size or weight, age, sex, time of onset, or family history, nor did we find any preoperative predictors in the 7 patients who developed moderate compensatory hyperhidrosis or in the 2 patients who developed severe compensatory hyperhidrosis. However, a general trend was noted—if patients sweat excessively before surgery in areas other than their palms, axillae, and feet, at room temperature, they have an increased likelihood of experiencing some degree of compensatory hyperhidrosis in these same areas after surgery. Of note, only 1 patient, regardless of the degree of compensatory hyperhidrosis as a result of the surgery, considered sweating to be moderately disagreeable in a temperature-controlled environment. In all other patients who had increased sweating in compensatory areas (thermoregulatory-driven), the increased sweating was primarily caused or exacerbated by heat or exercise. One of the 2 patients who regretted undergoing the procedure worked in a petroleum industry around an oil well, so heavy, hot, nonventilated garments made working conditions unbearable. However, his postoperative sweat pattern, documented by TST, showed his hands to be dry and his sweating to be minimal or normal in a temperature-controlled environment. All 155 patients had palmar successes at hospital discharge. Of note, the 5 patients in whom the surgery failed experienced failure within 18 months, and 3 experienced failure within 3 months postoperatively. These data suggest that a minimum of 18 months follow-up postoperatively may be necessary to determine failed procedures and patients with compensatory hyperhidrosis.

CONCLUSION

Long-term follow-up of sympathotomy for palmar-plantar hyperhidrosis, as conceived and performed in the Department of Neurosurgery at Mayo Clinic by T1-T2 sympathetic disconnection, laser Doppler blood flow monitoring, small single-incision uniportal access, and minimization of the size of the endoscope and cautery to less than the width of a pencil, revealed the following: no Horner syndrome, no intercostal neuralgia, no treated pneumothorax; 2 cases of hemothorax that required treatment (1 immediate, 1 delayed); minimal clinically detectable cardiovascular changes; 96.6% of patients experienced long-term satisfaction, with markedly decreased or absent sweating of the hands; 69.2% of patients experienced decreased axillary sweating; 39.8% of patients experienced decreased plantar sweating; no compensatory hyperhidrosis in 31.7% of patients; mild compensatory hyperhidrosis (no bother to the patient) in 62.2% of patients; moderate compensatory hyperhidrosis (patient requesting treatment) in 4.7% of patients; and severe compensatory hyperhidrosis (patient regrets undergoing the procedure) in 1.3% of patients. Of note, all mild, moderate, and severe cases of compensatory hyperhidrosis except one case were primarily thermoregulatory-driven and precipitated most commonly by a hot ambient temperature and/or exercise.

Our results compare favorably with or exceed those of other large series of patients in which different techniques were used. Highly selective T1-T2 sympathotomy for palmar hyperhidrosis offers a very high long-term success rate and, as importantly, a very low complication rate compared with other surgical techniques for this condition.

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EXHIBIT 5

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WAGNER, D K 7-354-496 Visit 3067 03/08/2013 - 03/14/2013 Mayo Clinic Rochester				
Previous Balance		$ 14,685.72		
06/20/13 Insurance Pmt		$ 338.30-		
06/20/13 Insurance Pmt		$ 589.76-		
06/20/13 Provider Liable		$ 416.40-		
06/20/13 Payer Contractual Adj		$ 41.80-		
06/20/13 Payer Contractual Adj		$ 82.09-		
	Visit Balance	$ 13,217.37		
	Insurance Pending		$ 13,217.37	
	Amount Due			$ 0.00
WAGNER, D K 7-354-496 Visit 3070 03/12/2013 - 03/12/2013 Saint Marys Hospital				
Previous Balance		$ 8,003.98		
	Visit Balance	$ 8,003.98		
	Insurance Pending		$ 8,003.98	
	Amount Due			$ 0.00
	Current Account Balance	$ 21,221.35		
	Insurance Claims Pending		$ 21,221.35	
	Current Amount Due			$ 0.00

0 5 3 2 1 9 8 3 6 8 1 4 6 8 9

BlueCross BlueShield of Illinois

June 14, 2013

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Identification Number:
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Claim Number: 3087553088U0H 00
Service Date: March 12, 2013

SUSAN WAGNER
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The clinical rational for the non-approval: NO DOC OF MEDICAL SEQUELAE SUCH AS RECURRENT SKIN MACERATIONS WITH BACTERIAL OR FUNGAL INFECTIONS, SECONDARY INFECTIONS, OR PERSISTENT ECZEMATOUS DERMATITIS IN SPITE OF MEDICAL TREATMENTS WITH TOPICAL DERMATOLOGICAL OR SYSTEMIC ANTICHOLINERGIC AGENTS.

If you have any questions, please feel free to contact us at (800) 730-8445, between the hours of 8 a.m. and 6 p.m., CST, Monday through Friday.

Sincerely,

Customer Advocate - U251127
Blue Cross and Blue Shield
Jacksonville Service Center

EXHIBIT 6

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DANIELLE-SUSANNE WAGNER
DOB: [redacted]

CINDY M. LEE, D.O.

01/02/2014

January 2, 2014

BCBSIL Claim Review Section

P.O. Box 2401

Chicago, Illinois 60690-1364

Group [redacted]

ID [redacted]

Patient Name: Danielle-Susanne Wagner

Date of Birth: [redacted]

Dear Illinois Appeals Department:

I am writing this on behalf of my patient, Danielle-Susanne Wagner, to document the medical necessity of treatment and surgical intervention using endoscopic transthoracic limited sympathotomy for palmar/plantar hyperhidrosis. This letter provides information about the patient's medical history and diagnosis and a statement summarizing my treatment rationale. Hyperhidrosis or excessive sweating can have a devastating effect on a patient's quality of life, causing physical discomfort, social embarrassment and disruption of occupational and daily activities. This certainly has done so in the life of Danielle-Susanne. There were numerous modalities that were tried to help the situation. She was tried on a couple different antidepressants and clonidine, without any improvement of her hyperhidrosis. She was given topical Drysol which was not effective. She was then sent for Botox injection, which was only minimally effective. This continued to disrupt the patient's quality of life and was a source of physical discomfort and embarrassment. The patient has suffered with this problem for years and as she became older, it became more of a medical and psychological insult. At that point, the patient was referred for a more aggressive treatment over conservative treatment. In light of this clinical information and my patients condition, the treatment options felt to be most helpful was this surgical intervention that Danielle-Susanne sought out with the help of her parents for endoscopic transthoracic limited sympathotomy to treat the palmar/plantar hyperhidrosis, and I believe this is a medically necessary treatment in this patient and warrants coverage. Please contact me at my office, 907-561-5007, if you require additional information.

Sincerely, Cindy M. Lee, DO.

Cindy M. Lee, DO

Cindy M. Lee, DO/ch/2234110

EXHIBIT 7